IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

JANSSEN PHARMACEUTICALS, INC., JANSSEN PHARMACEUTICA NV, and JANSSEN RESEARCH & DEVELOPMENT LLC, *Plaintiffs*, v. MYLAN LABORATORIES LIMITED, *Defendant*.	Civil Action No. 2:20-cv-13103 (EP)(LDW) FILED UNDER SEAL

PLAINTIFFS' PROPOSED FINDINGS OF FACT AND CONCLUSIONS OF LAW

TABLE OF CONTENTS

Page

TABLE OF CONTENTS
(continued)

Page

TABLE OF CONTENTS
(continued)

Page

TABLE OF CONTENTS
(continued)

Page

TABLE OF CONTENTS
(continued)

Page

TABLE OF CONTENTS
(continued)

Page

TABLE OF CONTENTS
(continued)

Page

TABLE OF CONTENTS
(continued)

Page

TABLE OF ABBREVIATIONS

Citations	
DTX	Defendant's Trial Exhibit (cites to PDF page number)
FOF	Plaintiffs' Proposed Findings Of Fact And Conclusions Of Law
FPTO	Final Pretrial Order, D.E. 99
PTX	Plaintiffs' Trial Exhibit (cites to PDF page number)
Tr.	Trial Transcript
Parties	
JPN	Janssen Pharmaceutica NV
JPI	Janssen Pharmaceuticals, Inc.
JRD	Janssen Research & Development, LLC
Mylan	Mylan Laboratories Limited
Patent-In-Suit	
693 Patent	U.S. Patent No. 10,143,693
Asserted Claims	Claims 5-7, 9-14
Representative Claims	Claims 5-7, 10 (as representative of claim 9), 11 (as representative of claim 12), 14 (as representative of claim 13)
Defined Abbreviations	
ANDA	Abbreviated New Drug Application
EPS	Extrapyramidal Symptoms
FDA	United States Food & Drug Administration

HCP	Healthcare Professional or Healthcare Practitioner or Healthcare Provider
IM	Intramuscular
LAI	Long-Acting Injectable
LAIA	Long-Acting Injectable Antipsychotic
NDA	New Drug Application
PK	Pharmacokinetics
Pop PK	Population Pharmacokinetics
POSA	Person of Ordinary Skill in the Art
PP	Paliperidone palmitate
PP1M	Paliperidone palmitate 1-month formulation
PP3M	Paliperidone palmitate 3-month formulation

TABLE OF MYLAN'S PROPOSED LABELS

Mylan's Proposed Labels		
ANDA No. 216228	PTX-92	Paliperidone palmitate 273 mg and 410 mg (or paliperidone 175 and 263 mg eq.)
ANDA No. 212290 (June 2020 version)	PTX-162	Paliperidone palmitate 546 mg (or paliperidone 350 mg eq.)
ANDA No. 212290 (Nov. 2022 version)	PTX-595	Paliperidone palmitate 546 mg (or paliperidone 350 mg eq.)
ANDA No. 215682	PTX-133	Paliperidone palmitate 819 mg (or paliperidone 525 mg eq.)

TABLE OF REFERENCES

References		
JAMA	PTX-113 DTX-26	Berwaerts et al., Efficacy and Safety of the 3-Month Formulation of Paliperidone Palmitate vs Placebo for Relapse Prevention of Schizophrenia, JAMA Psychiatry 72(8) (2015): 830-39
2014 Press Release	PTX-160 DTX-27	Janssen Investigational Treatment for Schizophrenia Shows Positive Efficacy, Delays Relapse (2014)
NCT-423	PTX-158 DTX-21	ClinicalTrials.gov archive, History of Changes for Study: NCT01515423, Study of Paliperidone Palmitate 3 Month and 1 Month Formulations for the Treatment of Patients With Schizophrenia
Invega Sustenna Label	PTX-106 DTX-25	Invega Sustenna Prescribing Information (Rev. 11/2014)
519 Publication	PTX-115 DTX-7	United States Patent Application Publication 2009/0163519 A1
536 Publication	PTX-116 DTX-97	United States Patent Application Publication 2011/0105536 A1
Samtani 2009	PTX-118 DTX-45	Samtani et al., Population Pharmacokinetics of Intramuscular Paliperidone Palmitate in Patients with Schizophrenia: A Novel Once-Monthly, Long-Acting Formulation of an Atypical Antipsychotic, Clin. Pharmacokinet 48(9) (2009): 585-600
Samtani 2011	PTX-161	Samtani et al., Dosing and Switching Strategies for Paliperidone Palmitate: Based on Population Pharmacokinetic Modelling and Clinical Trial Data, CNS Drugs 25(10) (2011): 829-845 and supplemental digital content
Rowland	PTX-145	Rowland and Tozer, Clinical Pharmacokinetics and Pharmacodynamics Concepts and Applications, 4th ed.

Abilify Maintena Label	PTX-168	Abilify Maintena (aripiprazole) Prescribing Information (Rev. 02/2013)
Risperdal Consta Label	PTX-187	Risperdal Consta Prescribing Information (Rev. 6/2014)
Osborne	DTX-36	Osborne et al., Health-related quality of life advantage of long-acting injectable antipsychotic treatment for schizophrenia: a time trade-off study, Health and Quality of Life Outcomes 10(35) (2012): 1-9

TABLE OF AUTHORITIES

Page(s)

Cases

TABLE OF AUTHORITIES
(continued)

Page(s)

TABLE OF AUTHORITIES
(continued)

Page(s)

TABLE OF AUTHORITIES
(continued)

Page(s)

TABLE OF AUTHORITIES
(continued)

Page(s)

TABLE OF AUTHORITIES
(continued)

Page(s)

TABLE OF AUTHORITIES
(continued)

Page(s)

Statutes

PROPOSED FINDINGS OF FACT

I. THE PARTIES, JURISDICTION, AND STANDING

1. Plaintiffs are Janssen Pharmaceuticals, Inc. ("JPI"),[1] Janssen Pharmaceutica NV ("JPN"), and Janssen Research & Development, LLC ("JRD"), collectively referred to as "Janssen." D.E. 99 ("FPTO") ¶¶ 1 n.1, 11, 14.

2. Defendant Mylan Laboratories Limited ("Mylan") is a generic drug manufacturer who has filed Abbreviated New Drug Application ("ANDA") Nos. 212290, 215682, and 216228, seeking approval from the United States Food & Drug Administration ("FDA") to market a generic version of Janssen's Invega Trinza product ("Mylan's Proposed ANDA Products"). FPTO ¶¶ 5, 33, 38, 43.

3. The parties have stipulated that "JPN is the owner of the entire right, title, and interest in and to the 693 Patent, as issued" and that JPI is the Invega Trinza New Drug Application ("NDA") holder. FPTO ¶¶ 11, 14; PTX-2, PTX-3, and PTX-4.[2]

II. SCIENTIFIC BACKGROUND

A. Schizophrenia and its Treatments

4. Schizophrenia is a serious and disabling mental illness that affects about 1% of the population. Tr. 175:5-6 (Berger); Tr. 870:13-16 (Kohler).

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[1] Abbreviations used herein are set forth in the above Table of Abbreviations.

[2] All pinpoint citations to exhibits in the record are to PDF page numbers unless otherwise indicated. All emphasis is supplied unless stated otherwise.

"Schizophrenia is a type of psychosis," *i.e.*, "loss of contact with reality." Tr. 176:1-8 (Berger). Core symptoms of the disease include positive symptoms (such as delusions, and hallucinations), negative symptoms (such as alogia and avolition), as well as cognitive and mood symptoms, which collectively affect the person's ability to manage their day-to-day responsibilities and to be successful in relationships, education, and employment. Tr. 54:9-55:6 (Sommi). Schizophrenia has a devastating impact on the patient's family and friends. Tr. 56:17-20 (Sommi). The disease also places a burden on society at large. Tr. 59:4-13 (Sommi).

5. There is no cure for schizophrenia. Tr. 176:9-11 (Berger). Rather, the goals of treatment are symptom improvement and relapse prevention, and these are namely obtained through the use of antipsychotic medication. Tr. 56:23-57:6, 58:1-13 (Sommi); Tr. 176:12-17 (Berger).

6. Antipsychotics are generally characterized as first- or second-generation. First-generation antipsychotics work by targeting dopamine and are associated with a high incidence of extrapyramidal side effects ("EPS"), such as acute dystonic reactions, pseudo-Parkinsonism, akathisia, and tardive dyskinesia. Tr. 59:16-61:20 (Sommi). EPS can be "very uncomfortable" and "distressing" and can lead to emergency room visits, hospitalization, and even suicide. Tr. 872:14-24, 875:23-24 (Kohler). Second-generation antipsychotics emerged in the 1980s; they work in part by targeting serotonin. Tr. 60:23-61:2 (Sommi); Tr. 177:18-20

(Berger). Though mitigating some of the EPS, second-generation antipsychotics additionally cause metabolic side effects, such as weight gain, increased risk of diabetes, and increase in blood glucose. Tr. 60:23-61:9 (Sommi).

7. Continuous treatment with antipsychotic medication is essential to staying well. Tr. 871:9-11 (Kohler). Stopping treatment could result in relapse. Tr. 871:11-14 (Kohler). With each relapse, the disease progresses with permanent loss of brain function and it becomes harder to treat. Tr. 68:18-69:5 (Sommi), 871:14-21 (Kohler).

B. Nonadherence and Long-Acting Injectables

8. Despite the need for continuous treatment, nonadherence is a particularly well-documented problem among patients suffering from schizophrenia. Tr. 182:15-17 (Berger); Tr. 67:3-8 (Sommi); Tr. 871:22-872:4 (Kohler); PTX-97 at 15-16. Among the many factors that contribute to poor adherence are medication-related side effects. Tr. 872:25-873:6 (Kohler); PTX-97 at 14. Accordingly, clinicians are keen to avoid overtreating patients, by using and dosing antipsychotic medications appropriately. Tr. 872:25-873:10 (Kohler).

9. Nonadherence may be improved with the use of long-acting injectable antipsychotics or "LAIAs." PTX-97 at 18 ("Schizophrenia treatment guidelines generally emphasize nonadherence . . . with oral antipsychotic agents as [one of] the most important reasons for LAI use."). First-generation LAIAs include Haldol

Decanoate and Prolixin Decanoate. Tr. 61:21-62:1 (Sommi). Second-generation LAIAs include Invega Trinza®, the three-month paliperidone product at issue here, Invega Sustenna®, the one-month formulation of paliperidone palmitate, as well as LAI formulations of risperidone, aripiprazole, and olanzapine. Tr. 62:25-63:2, 64:5-7 (Sommi). Only a few of the many oral antipsychotics are available as LAIAs. *See* Tr. 64:10-16 (Sommi).

10. In addition to improving adherence, LAIAs provide other advantages. Because they are administered less frequently, LAIAs offer patient convenience. Tr. 69:5-10 (Sommi). Studies also show that patients on LAIAs experience fewer relapses, which both delays neurodegeneration and improves prognosis. Tr. 68:13-69:5 (Sommi). LAIAs ease caretaker burden because, among other things, there are fewer discussions about medications and because LAIAs are administered to patients by healthcare professionals ("HCPs") who are better able to track medication adherence. Tr. 69:11-70:10 (Sommi). This facilitates better treatment decisions because HCPs can accurately assess whether and how the patient is responding to the medicine. Tr. 70:11-25 (Sommi).

11. Despite the benefits of LAIAs, the literature shows that HCPs may be reluctant to prescribe them. PTX-97 at 17. For example, "many clinicians lack knowledge about practical issues in the use of LAIAs, including dose selection,

pharmacokinetics, and what to do when a patient is late for an injection or has persistent symptoms after starting therapy." *Id.*; Tr. 891:20-892:3 (Kohler).

C. Pharmacokinetics and Population Pharmacokinetics

12. The development of dosing regimens for LAIAs implicates a field of science called pharmacokinetics. Pharmacokinetics is the study of "what the body does to a drug" through four processes: absorption, distribution, metabolism, and excretion. Tr. 806:23-807:8 (Gobburu); Gobburu Demonstratives Slide 3.

13. Monitoring pharmacokinetics requires obtaining drug levels, by taking blood samples from patients, and measuring drug levels at various time points. Tr. 807:9-11 (Gobburu). An individual's serum drug levels are then plotted on a plasma concentration time curve. Tr. 807:11-13 (Gobburu).

14. An individual's response to a drug is unpredictable. Tr. 807:5-19 (Gobburu); PTX-145 at 500. The reasons for this variability "are manifold and include genetics, disease, age, gender, body weight, drugs given concomitantly, and various behavioral and environmental factors." PTX-145 at 500.

15. Population pharmacokinetics ("pop-PK"), used in designing dosing regimens, accounts for these variations and allows scientists to "understand not only the average . . . but the spread of the data." Tr. 808:21-809:5 (Gobburu).

III. INVEGA TRINZA

16. Invega Trinza is a three-month LAI formulation of the second-generation antipsychotic paliperidone palmitate. Tr. 73:22-25, 74:8-11 (Sommi). At the time of its approval in May 2015, Invega Trinza was lauded as "a revolutionary drug." PTX-226 at 5. It was the first—and remains the only—LAIA that is administered once every three months. Tr. 74:23-75:6 (Sommi); PTX-226 at 5.

17. When Invega Trinza was introduced, HCPs had no experience with an LAIA dosed at three months. Tr. 874:22-875:1 (Kohler); Tr. 74:23-75:2 (Sommi). HCPs had concerns about the dose of Invega Trinza being administered to the patient—wondering whether such a dose will be large enough to remain effective for three months and whether such a dose will be so large to cause delayed and prolonged side effects. Tr. 875:1-24 (Kohler); Tr. 1058:15-16 (Berger). With a three-month product, HCPs recognized that they may have to manage side effects "over a much longer period of time." Tr. 875:16-24 (Kohler).

18. Since its approval, "Invega Trinza has been very well received." Tr. 876:2-4 (Kohler). Invega Trinza "has fulfilled [HCPs'] expectations in providing effective treatment over a period of at least three months in people who were previously stabilized . . . [on] Invega Sustenna" and has demonstrated a "tolerable side effects profile." Tr. 876:4-9 (Kohler). Mylan's expert, Dr. Berger, agrees that

Invega Trinza (a PP3M) is "a wonderful drug." Tr. 241:20-21; Tr. 243:23-24 (Berger).

IV. THE 693 PATENT

19. The 693 Patent "relates to a method for treating patients who have missed a treatment of 3-month paliperidone palmitate extended-release injectable suspension formulation" or "PP3M." PTX-1 at 1:15-19, 17:16; Tr. 76:17-76:18 (Sommi). The Asserted Claims describe dosing regimens for administering injectable paliperidone palmitate to a patient that had been last administered PP3M 4 to 9 months ago. *See, e.g.*, PTX-1 at Claim 5.

A. Prosecution History

20. On April 5, 2016, Janssen filed the application that matured into the 693 Patent. FPTO ¶ 13. The application included claims 1-8. DTX-8 at 40-42.

21. On November 1, 2017, the Patent Office Examiner conducted prior art searches on the East and Google Scholar databases.[3] DTX-8 at 193. Although the search terms used on Google Scholar are not recorded, the Examiner's search queries on East included "paliperidone," "three month," and the inventor names. DTX-8 at 205-06.

[3] Dr. Forrest agreed that Google Scholar includes articles published in the Journal of the American Medical Association, such as the publication referred to as "JAMA" (PTX-113) in this litigation. Tr. 691:2-4 (Forrest); FOF 110.

22. On November 20, 2017, the Examiner rejected claims 1-8 as obvious over the 536 Publication in view of Osborne, and on the ground of nonstatutory obviousness-type double patenting over claims 1-16 of US Patent No. 9,439,906 (the 906 Patent) in view of Osborne. DTX-8 at 196-203 (Non-Final Office Action). The 906 Patent covers dosing regimens for initiating patients on PP1M. There was no rejection under 35 U.S.C. § 112. *Id.*; Tr. 768:1-11 (Forrest).

23. In response to the double patenting rejection, Janssen pointed out that the 906 Patent concerned PP1M and not PP3M. "The instant claims are solely directed to what patients should do if a dose of ***PP3M*** is missed and they desire getting back on the medication. These methods are patentabl[y] distinct from how a patient should initially get onto PP1M." *Id.* at 217.

24. On June 14, 2018, the Examiner conducted updated searches on East and Google Scholar. *Id.* at 236. The search queries on East again included "paliperidone," "three month," and the inventors' names. *Id.* at 237.

25. On June 27, 2018, the PTO issued a Notice of Allowance, concluding that the claims of the 693 Patent are patentable. DTX-8 at 223. The PTO reasoned:

> While the closest prior art of '536 publication teaches a dosing regimen for a patient to get back onto PP1M after missed dose of PP1M, the prior art does not teach 3-month injectable paliperidone palmitate depot (PP3M) and exact numbers of reinitiation loading doses and maintenance doses and their amounts for patients who had been treated with a PP3M and had been last administered the PP3M more than 9 months or 4 to 9 months ago as claimed. No other prior art was found to teach that

> when a patient misses a dose of PP3M for extended period of time a patient must first be treated and stable on PP1M and then a PP3M injection is then given at the time that the patient would have received their next PP1M injection as claimed. Thus, the instant claims are novel and non-obvious over the prior art."

Id. at 229.

26. The 693 Patent issued on December 4, 2018. FPTO ¶ 2.

B. The Patent Specification

27. As the specification of the 693 Patent explains, PP3M "offers the prospect of fewer opportunities for nonadherence than currently available long acting injectable formulations, thus reducing relapse risk as a result of subtherapeutic plasma concentration and its associated negative consequences in patients with schizophrenia." PTX-1 at 2:15-19.

28. But "[e]ven with a drug administered once every 3 months . . . , patients at time miss their doses of medication." *Id.* at 2:20-22. "Consequently, there is a need to reinitiate a dosing regimen for patients who miss their regularly scheduled dose of medication." *Id.* at 2:22-24. "Thus, the objective of the present application is to provide a ***dosing regimen of paliperidone palmitate*** for patients in need of a treatment who have missed their 3 month (±2 weeks) dose of paliperidone palmitate 3-month extended-release injectable suspension." *Id.* at 2:24-29.

29. The specification then summarizes the claimed dosing regimens. *Id.* at 2:32-3:56. Relevant to the Asserted Claims, the specification describes a "dosing regimen for administering an injectable paliperidone palmitate depot to a patient in

need of psychiatric treatment that has been treated with" PP3M, "wherein said patient misses for a period of between about four months and about nine months" the "next scheduled maintenance dose" of PP3M. *Id.* at 2:32-42. The claimed dosing regimens "compris[e]" three numbered doses of PP1M or PP3M, corresponding to the Asserted Claims. *See* FOF 67.

30. In addition to describing the claimed dosing regimens, the specification provides detailed information about PP1M and PP3M formulations for use in the dosing regimens. The specification discloses the "composition for the 1-month formulation," which describes the active ingredient (paliperidone palmitate), the types of inactive ingredients, the concentrations of the ingredients, as well as the "composition" of the 3-month formulation. PTX-1 at 13:49-56, 13:62-14:3. It provides the average particle size range for both PP1M (2,000-100 nm) and PP3M (20-3 μm), as well as preferred particle size ranges of 9 μm to 4 μm for PP3M and 1,400 to 900 nm for PP1M. PTX-1 at 9:39-51. In addition to describing the structural features of PP1M and PP3M, the specification provides manufacturing instructions for making PP1M and PP3M. *See id.* at 11:23-29; 11:50-12:35.

31. The 693 Patent also provides examples of PP1M and PP3M formulations, for which the specific inactive ingredients are disclosed, *e.g.*, *id.* at 4:33-39, 13:56-62, and describes Invega Sustenna as a commercial embodiment of

PP1M and Invega Trinza as a commercial embodiment of PP3M. *Id.* at 4:18-20, 5:23-25, 5:44-46, 6:63-65.

32. To devise the claimed dosing regimens, the inventors of the 693 Patent developed a "comprehensive population pharmacokinetics (PK) model" for paliperidone palmitate and used that model to simulate various dosing regimen scenarios. *Id.* at 17:25-46, 19:55-20:28, Figs. 4A-4C.

C. The Asserted Claims

33. The Asserted Claims of the 693 Patent include independent claim 5 and dependent claims 6-7 and 9-14. All dependent claims depend directly or indirectly from claim 5. *See* PTX-1 at 21:10-22:3.

34. Claim 5 claims:

> A dosing regimen for administering an injectable paliperidone palmitate depot to a patient in need of treatment for psychosis, schizophrenia or bipolar disorder that has been treated with PP3M, wherein said patient had been last administered a PP3M injection 4 to 9 months ago and the next scheduled maintenance dose of PP3M should be administered to said patient, comprising:
>
> (1) administering intramuscularly in the deltoid muscle of said patient a first reinitiation loading dose of PP1M;
>
> (2) administering intramuscularly in the deltoid muscle of said patient a second reinitiation loading dose of PP1M on about the 4th day to about the 12th day after administering of said first reinitiation loading dose; and
>
> (3) administering intramuscularly in the deltoid or gluteal muscle of said patient a reinitiation dose of PP3M on about the 23rd day to about the 37th day after administering the second

reinitiation loading dose of PP1M wherein said first and second reinitiation loading doses and the reinitiation PP3M dose are selected from the table below based on the amount of the missed dose

Missed Dose of PP3M	Reinitiation Doses of PP1M	Reinitiation Doses of PP3M
175 mg eq.	50 mg eq.	175 mg eq.
263 mg eq.	75 mg eq.	263 mg eq.
350 mg eq.	100 mg eq.	350 mg eq.
525 mg eq.	100 mg eq.	525 mg eq.

PTX-1 at 21:10-39.

35. Claims 6-7 depend directly from claim 5 and narrow this method to a specific patient in need of treatment for psychosis and schizophrenia, respectively. *Id.* at 21:40-43; Tr. 100:10-25 (Sommi).

36. Claim 9 depends directly from claim 5 and narrows this method to a specific time for the administering of the second reinitiation dose of PP1M to "about 7 days" after the first reinitiation loading dose of PP1M. PTX-1 at 21:46-48. Claim 10 depends from claim 9 and narrows this method to a specific time for the administering of the second reinitiation dose of PP1M to "7 days" after the first reinitiation loading dose of PP1M. *Id.* at 24:49-51; Tr. 101:7-14 (Sommi).

37. Claim 11 depends directly from claim 5 and narrows this method to a specific time for the administering of the reinitiation dose of PP3M to "about 30 days" after the second reinitiation loading dose of PP1M. PTX-1 at 21:52-54; Tr.

101:24-102:4 (Sommi). Claim 12 depends from claim 11 and narrows this method to a specific time for the administering of the reinitiation dose of PP3M to "30 days" after the second reinitiation loading dose of PP1M. PTX-1 at 21:55-57.

38. Claim 13 depends directly from claim 5 and narrows this method to a specific time for the administering of the reinitiation dose of PP3M to "about a month" after the second reinitiation loading dose of PP1M. *Id.* at 21:58-60. Claim 14 depends from claim 11 and further narrows this method to a specific time for the administering of the reinitiation dose of PP3M to "a month" after the second reinitiation loading dose of PP1M. *Id.* at 22:1-3; Tr. 102:4-5 (Sommi).

D. The Dosing Instructions for Invega Trinza Track the Asserted Claims

39. The 693 Patent covers Invega Trinza. FPTO ¶ 4. The Invega Trinza label includes instructions that map directly on the Asserted Claims of the 693 Patent. PTX-43 at 3, 5-6; Tr. 88:14-92:8 (Sommi); *see also* Tr. 245:5-9, 21-23 (Berger). In particular, the Invega Trinza label instructs HCPs that if a patient had their last dose of Invega Trinza between 4 and 9 months ago, "***do NOT*** administer the next dose" of Invega Trinza. PTX-43 at 5. "Instead, use the re-initiation regimen shown in Table 2." *Id.* Table 2, in turn, tracks perfectly with the Asserted Claims. Tr. 88:14-92:8 (Sommi); *see also* Tr. 244:14 (Berger).

V. MYLAN'S PROPOSED LABELS INDUCE HEALTHCARE PROVIDERS TO INFRINGE THE ASSERTED CLAIMS

A. Mylan's ANDA Products

40. "Mylan filed ANDA No. 216228 with the FDA seeking approval to market and sell within the United States Mylan's Proposed ANDA Products (273 mg/0.875 mL and 410 mg/1.315 mL)." FPTO ¶ 43. The 273 mg and 410 mg paliperidone palmitate dose strengths are equivalent to 175 and 263 mg paliperidone. Tr. 94:12-16 (Sommi). As part of ANDA No. 216228, Mylan submitted a proposed label, PTX-92, for FDA approval. Tr. 94:9, 12-16 (Sommi).

41. "Mylan filed ANDA No. 212290 with the FDA seeking approval to market and sell within the United States Mylan's Proposed ANDA Product (546 mg/1.75 mL)." FPTO ¶ 33. The 546 mg paliperidone palmitate dose strength is equivalent to 350 mg dose strength of paliperidone. Tr. 94:17-19 (Sommi). As part of ANDA No. 212290, Mylan submitted a proposed label, PTX-162, for FDA approval. Tr. 94:9, 17-19 (Sommi).

42. "Mylan filed ANDA No. 215682 with the FDA seeking approval to market and sell within the United States Mylan's Proposed ANDA Product (819 mg/2.625 mL)." FPTO ¶ 38. The 819 mg paliperidone palmitate dose strength is equivalent to 525 mg dose strength of paliperidone. Tr. 94:20-23 (Sommi). As part of ANDA No. 215682, Mylan submitted a proposed label, PTX-133, for approval. Tr. 94:9, 20-23 (Sommi).

B. Mylan's Proposed Labels

43. The proposed labels submitted in connection with ANDA Nos. 216228, 212290, and 215682 are collectively referred to as "Mylan's Proposed Labels." For purposes of determining infringement, Dr. Sommi analyzed Mylan's Proposed Labels and determined that the labels are the same in material respects. Tr. 94:24-95:3, 98:18-99:4 (Sommi).

44. [redacted] FPTO ¶ 25.

45. [redacted] PTX-92 at 1; PTX-133 at 1; PTX-162 at 1; PTX-595 at 5.

46. [redacted]

[redacted]

PTX-92 at 6; PTX-133 at 6; PTX-162 at 6; *see also* PTX-595 at 14.

47. [redacted]

[redacted]

PTX-92 at 7; PTX-133 at 7; PTX-162 at 7; *see also* PTX-595 at 15.

48. On November 15, 2022, Mylan produced to Janssen an updated proposed label that it had submitted to the FDA. *See* PTX-595; Tr. 103:19-21. The changes to Mylan's Proposed Labels, reflected in PTX-595, do not impact the infringement analysis. Tr. 105:6-7, 106:13-15 (Sommi).

C. Mylan's Proposed Labels Recite Each Limitation of the Representative Claims

49. [redacted]

[redacted] Tr. 99:19-21 (Sommi); Tr. 1038:2-14

(Berger) [redacted]

50. [redacted] Tr. 261:7-13 (Berger), Tr. 98:14 (Sommi).

1. Claim 5

51. **A Dosing Regimen.** Claim 5 claims a dosing regimen. PTX-1 at 21:10-11 ("A dosing regimen for administering an injectable paliperidone palmitate depot…"); Tr. 79:25-80:3, 97:17-21, 116:1-2 (Sommi); Tr. 285:7-9 (Berger). [redacted]

52. **For a Patient in Need of Treatment for Psychosis, Schizophrenia or Bipolar Disorder.** Claim 5 identifies a patient in need of treatment for psychosis, schizophrenia or bipolar disorder. PTX-1 at 21:11-12 ("to a patient in need of treatment for psychosis, schizophrenia"); Tr. 78:10-12, 97:19-98:3

(Sommi). Mylan's Proposed Labels also identify a patient in need of treatment for schizophrenia. PTX-92 at 4; PTX-133 at 4 (same); PTX-162 at 4 (same); PTX-595 at 9 (same); Tr. 97:19-98:3 (Sommi).

53. **For a Patient Who Has Been Treated with PP3M, Had Been Last Administered PP3M Four to Nine Months Ago, and the Next Scheduled Maintenance Dose of PP3M Should Be Administered to Said Patient.** Claim 5 identifies a patient who has been treated with PP3M and had been last administered PP3M four to nine months ago. PTX-1 at 21:11-14 ("to a patient . . . that has been treated with PP3M, wherein said patient had been last administered a PP3M injection 4 to 9 months ago and the next scheduled maintenance dose of PP3M should be administered to said patient"); Tr. 78:10-12, 82:2-8, 125:19-22 (Sommi), 240:25-241:3 (Berger). Mylan's Proposed Labels also identify a patient who has been treated with PP3M and had been last administered a dose of PP3M four to nine months ago. PTX-92 at 6-7; PTX-133 at 6-7; PTX-162 at 6-7; PTX-595 at 14-15; Tr. 97:25-98:3, 106:2-15 (Sommi).

54. **Administering a First Reinitiation Loading Dose of PP1M.** Claim 5 identifies the first step of the claimed dosing regimen as "**(1)** administering intramuscularly in the deltoid muscle of said patient a first reinitiation loading dose of PP1M." PTX-1 at 21:17-18; Tr. 98:4-6, 123:9-12 (Sommi). [redacted]

[redacted]

[redacted]

PTX-92 at 7 (Table 2); PTX-133 at 7 (same); PTX-162 at 7 (same); PTX-595 at 15; Tr. 98:6-8 (Sommi).

55. **Administering a Second Reinitiation Dose of PP1M.** Claim 5 identifies the second administering step of the claimed dosing regimen as "**(2)** administering intramuscularly in the deltoid muscle of said patient a second reinitiation loading dose of PP1M on about the 4th day to about the 12th day after administering of said first reinitiation loading dose." PTX-1 at 21:19-22; Tr. 98:6-9 (Sommi). [redacted]

[redacted]; PTX-133 at 7 (same); PTX-162 at 7 (same); PTX-595 at 15; Tr. 98:6-9 (Sommi).

56. **Administering a Reinitiation Dose of PP3M.** Claim 5 identifies the third administering step of the claimed dosing regimen as "**(3)** administering intramuscularly in the deltoid or gluteal muscle of said patient a reinitiation dose of PP3M on about the 23rd day to about the 37th day after administering the second

reinitiation loading dose of PP1M." PTX-1 at 21:23-26; Tr. 98:10-13, 124:21-23 (Sommi). [redacted] PTX-133 at 7 (same); PTX-162 at 7 (same); PTX-595 at 15; Tr. 98:10-13 (Sommi).

57. **Dose Amount of Reinitiation Doses.** The table in Claim 5 provides the dose amounts for the reinitiation doses of PP1M and PP3M:

Missed Dose of PP3M	Reinitiation Doses of PP1M	Reinitiation Doses of PP3M
175 mg eq.	50 mg eq.	175 mg eq.
263 mg eq.	75 mg eq.	263 mg eq.
350 mg eq.	100 mg eq.	350 mg eq.
525 mg eq.	100 mg eq.	525 mg eq.

PTX-1 at 21:31-39; Tr. 98:14-17, 127:3-22 (Sommi). The dose amounts for the reinitiation doses are based on the amount of the missed dose of PP3M. PTX-1 at 21:27-29 ("wherein said first and second reinitiation loading doses and the reinitiation PP3M dose are selected from the table below based on the amount of the missed dose"); Tr. 78:24-79:4 (Sommi). [redacted]

PTX-92 at 7; PTX-133 at 7; PTX-162 at 7; PTX-595 at 15; Tr. 98:14-17 (Sommi). The dose amounts of the reinitiation doses are similarly based on the amount of the last dose of PP3M and track the amounts in claim 5. PTX-92 at 7; PTX-133 at 7; PTX-162 at 7; PTX-595 at 15; Tr. 98:14-17 (Sommi).

2. Claims 6 and 7

58. **Wherein The Patient Is In Need of Treatment for Psychosis.**

Claim 6 is "[t]he method of claim 5, wherein said patient is in need of treatment for psychosis." PTX-1 at 21:40-41; Tr. 100:13-25 (Sommi). Patients with schizophrenia have psychosis and will therefore be in need of treatment for psychosis. Tr. 100:18-25 (Sommi); *see also* Tr. 176:8 (Berger) ("Schizophrenia is a type of psychosis."). Accordingly, Mylan's Proposed Labels also identify a patient in need of treatment for psychosis. PTX-92 at 4; PTX-133 at 4; PTX-162 at 4; Tr. 97:17-98:3, 100:18-101:6 (Sommi).

59. **Wherein The Patient Is In Need of Treatment for Schizophrenia.** Claim 7 is "[t]he method of claim 5, wherein said patient is in need of treatment for schizophrenia." PTX-1 at 21:42-43; Tr. 100:16-101:6 (Sommi). Mylan's Proposed Labels also identify a patient in need of treatment for schizophrenia. PTX-92 at 4; PTX-133 at 4; PTX-162 at 4; Tr. 97:17-98:3, 100:18-101:6 (Sommi).

3. Claim 10

60. **Timing of Second Reinitiation Dose.** Claim 10 is "[t]he method of claim 9, wherein the second reinitiation dose of PP1M is administered 7 days after administering said first reinitiation loading dose of PP1M." PTX-1 at 21:49-51. Claim 10 specifies that the second step of the claimed dosing regimen is seven days after the first reinitiation loading dose. Tr. 101:7-14 (Sommi). [redacted] PTX-133 at 7 (same); PTX-162 at 7 (same); PTX-595 at 15; Tr. 101:10-23 (Sommi).

4. Claims 11 and 14

61. **Timing of Second Reinitiation Dose.** Claim 11 is "[t]he method of claim 5, wherein the reinitiation dose of PP3M is administered about 30 days after

administering said second reinitiation loading dose of PP1M." PTX-1 at 21:52-54. Claim 11 specifies that the third step of the claimed dosing regimen is about 30 days after the second reinitiation loading dose of PP1M. Tr. 102:3-13 (Sommi).

[redacted] PTX-133 at 7 (same); PTX-162 at 7 (same); PTX-595 at 15 (same); Tr. 98:10-13, 101:24-102:22 (Sommi).

62. **Timing of Third Reinitiation Dose.** Claim 14 is "[t]he method of claim 11[,] wherein the reinitiation dose of PP3M is administered a month after administering said second reinitiation loading dose of PP1M." PTX-1 at 22:1-3. Claim 14 specifies that the third step of the claimed dosing regimen is about a month after the second reinitiation loading dose of PP1M. Tr. 102:4-13 (Sommi).

[redacted]

[redacted] PTX-133 at 7 (same); PTX-162 at 7 (same); PTX-595 at 15 (same); Tr. 98:10-13, 101:24-102:22 (Sommi).

D. A Single Entity—a Healthcare Provider—Performs the Three Steps of the Claimed Dosing Regimens

63. Having no choice but to concede that its Proposed Labels instruct every element of the Asserted Claims, Mylan contends that there will be no direct infringement because the steps of the claimed dosing regimens will be carried out by two independent actors: the patient, who missed a dose of PP3M and returned for treatment three times, and their HCPs, who administer the claimed dosing regimen. Tr. 172:24-173:7 (Berger). This contention is referred to as the "divided infringement issue." Tr. 204:7-10 (Berger).

64. Mylan did not disclose its divided infringement defense in its May 26, 2021, Non-Infringement Contentions. *See* D.E. 81-3. At five pages long, Mylan's Non-Infringement Contentions presented two theories: Mylan does not directly infringe the Asserted Claims because Mylan itself does not administer the claimed dosing regimen to the patient; and Mylan does not indirectly infringe the claims because it does not have any control over whether patients are treated with the dosing regimen. *See id.* The contentions do not contain the words "divided infringement," cite no case law on divided infringement, and do not assert that the Asserted Claims have seven steps. *See id.* Mylan did not seek to amend its Non-

Infringement Contentions to add a divided infringement defense. Mylan first disclosed such a defense in Dr. Berger's expert report. *See* D.E. 72-12.

65. The premise of Mylan's divided infringement theory is that the method of treatment set forth in the Asserted Claims has "seven steps." Tr. 186:10-188:19; 287:15-20 (Berger). In contrast, Janssen's infringement theory is based on the position that the Asserted Claims comprise three steps of administering the three reinitiation doses numbered as "(1)," "(2)," and "(3)" in the language of the claims. Tr. 79:5-86:25 (Sommi); Sommi Infringement Demonstratives Slide 5.

66. As there is no dispute that the three numbered reinitiation doses recited in the Asserted Claims will be administered by a single actor—*i.e.*, an HCP, Tr. 123:13-18 (Sommi); Tr. 291:5-8 (Berger); FOF 89—Mylan's divided infringement theory fails.

1. The Claimed Dosing Regimens Have Three Steps

a. The Language of the Asserted Claims Identifies Three Steps to the Claimed Dosing Regimens

67. As recited in the plain language of the Asserted Claims, the claimed dosing regimens "compris[e]" three steps: "administering" the three "reinitiation" doses that are enumerated (1), (2), and (3) in claim 5. PTX-1 at 21:17-29 ("(1) administering . . . ; (2) administering . . . ; (3) administering . . . ."); Tr. 79:5-14; 98:4-17, 115:25-116:2, 125:19-22 (Sommi). As Dr. Sommi testified, "this is a dosing regimen ***for administering*** PP3M that's comprising ***these three steps*** for the

patient that's been specified as having schizophrenia or had their injection four to nine months ago." Tr. 79:25-80:3 (Sommi).

68. There is no dispute that the claims ***require*** a patient having missed a dose of PP3M and having "had been last administered a PP3M injection 4 to 9 months ago." PTX-1 at 21:13-14; Tr. 85:3-13 (Sommi); Tr. 285:22-286:9 (Berger).

69. But as Dr. Sommi testified, this requirement—"wherein said patient had been last administered a PP3M injection 4 to 9 months ago"—is a "descriptor of the clinical situation" in which the claimed dosing regimens are to be administered—not a step of the claimed regimens.[4] *See* Tr. 82:1-8, 85:10-18, 86:13-18, 125:19-22 (Sommi).

70. The language of the Asserted Claims makes this clear. The Asserted Claims claim a "***dosing regimen*** for administering an injectable paliperidone palmitate depot . . . comprising" the administration of three "***dose[s]***" numbered "(1)," "(2)," and "(3)." PTX-1 at 21:17-29; Tr. 84:9-21 (Sommi). The claims provide that this dosing regimen is administered "***to*** a patient" who meets certain criteria, including having "been last administered a PP3M injection 4 to 9 months ago." PTX-1 at 21:10-16; Tr. 84:22-85:2 (Sommi).

[4] The Asserted Claims recite various elements or limitations of the claims, *see* FOF 51-62, but the "administering" steps are the only ***steps*** of the claimed dosing regimens.

71. The language of the Asserted Claims is typical of dosing regimens for drug products. "[O]ften, if not always," dosing instructions for a drug product separately identify the dosing regimen to be administered, and the "criteria" for determining whether to administer the dosing regimen to a particular patient. Tr. 85:10-22 (Sommi).

72. Furthermore, the past-tense language of the claims makes clear that the patient missed a dose and returned for treatment ***before*** the claimed dosing regimens are administered. PTX-1 at 21:13-15 ("wherein said patient ***had been last administered*** a PP3M injection ***4 to 9 months ago***").

73. Mylan's expert, Dr. Berger, ignored the grammatical tense of the claims as "irrelevant" to his non-infringement opinions. Tr. 286:13-17 (Berger) ("Whether it's past tense, future tense, present tense, the tense of the verb is irrelevant."). Then, in direct contrast to basic tenets of the English language, he asserted that the "wherein said patient ***had last been administered*** PP3M four to nine months ago" clause is stated in the "present tense." Tr. 286:20-24 (Berger).

74. On cross-examination, Dr. Berger conceded that the claim language recites only three steps, but Dr. Berger's view is that the claim language "is not correct." Tr. 290:1-2 (Berger) ("The claim is not correct when ***it says there's only three steps***."); Tr. 287:19-20 (Berger) ("***The claim lists three steps in writing, however***, as I testified, there are seven steps to this claim."). The apparent

reasoning for his position was that "for ***any*** treatment that[i]s administered by a health care professional at a health care facility," patients "have to show up." Tr. 297:2-11 (Berger).

75. Mylan's invalidity expert, Dr. Forrest, agrees that, as written, the steps of the Asserted Claims consist of administering the reinitiation doses. Tr. 741:1-6 (Forrest) ("**Q.** . . . [A]fter a patient received a dose of PP3M, if they come back within four to nine months, ***the first step of the claimed missed dose regimen is give them PP1M***, right? **A.** ***That is correct***."). Nowhere in Dr. Forrest's obviousness analysis did he endorse or even address the three supposed "return to treatment" steps that Dr. Berger posited. FOF 109 n.7.

76. Dr. Berger relies on a misunderstanding of the law in reaching his opinion on the meaning claims, believing that it is not the claims but "the patent [that] defines the metes and bounds of the patent." Tr. 284:17-20 (Berger).

77. Dr. Berger also made the illogical inference that if the patient takes action to become part of the patient population, that action must be a step of the method of treatment. *See* Tr. 189:20-190:22 (Berger). Thus, according to Dr. Berger, overdosing would be the first step in a dosing regimen for a drug indicated to treat overdose. Tr. 297:12-24 (Berger). This opinion is unreasonable.

b. The Patent's Specification Is Consistent with the Plain Language of the Claim

78. Dr. Berger relies on statements from the patent specification to suggest that the claimed dosing regimens have more than three steps. *See* Tr. 192:3-193:23 (Berger). The specification is, however, entirely consistent with the claimed dosing regimens comprising only three steps.

79. For example, Dr. Berger refers to the title of the 693 Patent ("Dosing Regimen for Missed Doses for Long-Acting Injectable Paliperidone Esters") and the abstract ("The present application provides a method for treating patients in need of psychiatric treatment, wherein said patient is being treated with the 3-month formulation of paliperidone palmitate and fails to take the next scheduled dose . . . ."), testifying that the claims require "patient action for this patent to come into play." Tr. 192:9-22 (Berger).

80. Similarly, Dr. Berger cites a portion of the summary of the invention, which refers to "a dosing regimen for administering an injectable paliperidone palmitate depot to a patient . . . wherein said patient misses for a period of between about four months and about nine months . . . the next scheduled maintenance dose . . . ." *See* PTX-1 at 2:34-41. According to Dr. Berger, "[t]hat says patient misses. That's patient action. Patient has to do that in order for this patent to come into play." Tr. 193:10-19 (Berger).

81. But these portions of the specification simply confirm that the patient must have missed a dose by a certain amount of time before the dosing regimen of the claims is to be administered, what Dr. Sommi referred to as "criteria" or the "clinical situation" to be addressed by the claimed dosing regimens. *See* Tr. 82:2-8, 85:10-18 (Sommi); FOF 68-69. This does not suggest that missing a dose is a ***step*** of the claimed dosing regimens.

c. The Prosecution History Is Consistent with the Plain Language of the Asserted Claims

82. The statements from the prosecution history about which Dr. Berger testified similarly describe the clinical situation addressed by the claimed dosing regimens. Tr. 194:16-197:17 (Berger).

83. During prosecution of the 693 Patent, the Patent Examiner initially rejected the claims as obvious over the 536 Publication (a PP1M reference) in view of Osborne, DTX-8 at 197, and for obviousness-type double patenting over the 906 Patent (the patent that issued from the 519 Publication, a PP1M reference) in view of Osborne, *id.* at 202. (The Examiner later withdrew those rejections and allowed the claims. *Id.* at 227-29.) According to the Examiner, Osborne disclosed that "new medications that can be administered over 3 monthly intervals are in development" and determined that "the best time intervals for injection [of] antipsychotic medicines including paliperidone palmitate, were three month intervals." *Id.* at 199.

84. In response to these initial rejections, Janssen explained, consistent with Dr. Sommi's testimony, that the "situation" addressed by the Asserted Claims was when a patient has missed a dose of PP3M by a month or more:

> The currently pending claims are directed to methods of getting patients back onto a [PP3M] when a dose has been missed by a month or more. ***In that situation, the patient cannot just be given a PP3M injection and continue with the medication. A reinitiation dosing regimen must be administered*** that includes some administration of [PP1M] before getting back onto PP3M.

Id. at 214.

85. Dr. Berger cited the first sentence of the above passage—emphasizing the words "has been missed"—to suggest that "patient action is required." Tr. 196:8-15 (Berger). But the dispute is whether the act of having missed a dose is a step of the claimed dosing regimens, as Dr. Berger opined, or rather a "descriptor of the clinical situation" in which the claimed dosing regimens is administered, as Dr. Sommi opined. *See* Tr. 82:2-8 (Sommi). The prosecution history refers to having missed a dose as a clinical "situation," *see* DTX-8 at 214, and thus supports Dr. Sommi's opinion.

86. Dr. Berger also pointed out that "Janssen distinguished itself from Osborne by focusing on reinitiation and specifically on the patient missing the dose and the patient wishes to get back on that medication. That's what this patent is directed toward." Tr. 196:25-197:5; DTX-8 at 216. But once again, this is entirely consistent with the plain language of the claim and with Janssen's position. The

claims do address "what to do if a patient missed a dose of [PP3M] and wishes to get back onto that medication." DTX-8 at 216. They call for administering the claimed dosing regimens in that situation. *Id.*; Tr. 82:3-8 (Sommi). Nothing in this passage indicates that a patient missing a dose or wishing to get back onto medication is a ***step*** of the claimed dosing regimen.

87. Similarly, Janssen's statement to the Examiner that "[t]he instant claims are solely directed to what patients should do if a dose of PP3M is missed and they desire getting back on the medication" does not support Mylan's position. DTX-8 at 217; *see* Tr. 195:8-196:5 (Berger); Tr. 32:4-16 (Mylan's opening). This passage does not state that missing a dose is a step in the claimed method of treatment. To the contrary, it states that the claims are directed to what happens "***if*** a dose of PP3M is missed." DTX-8 at 217. This is consistent with Janssen's position that a patient having missed a dose is the "clinical situation" addressed by the Asserted Claims. *See* Tr. 82:1-8 (Sommi). Janssen has never disputed that the Asserted Claims are directed "solely" to that situation. *See, e.g.*, Tr. 85:3-13 (Sommi).

2. Healthcare Providers Carry Out All Three Steps of the Claimed Dosing Regimens

88. Once it is determined that the claimed dosing regimens have three steps, Mylan's divided infringement non-infringement theory fails on the undisputed facts. It was undisputed that each of the three listed administering steps

in the Asserted Claims is performed by an HCP. Tr. 96:23-97:7, 146:10-15 (Sommi); Tr. 291:5-8 (Berger).

89. [redacted]; PTX-162 at 4 (same); PTX-595 at 6 (same); Tr. 139:3-7 (Sommi). And the experts agreed that, in practice, Mylan's Proposed ANDA Products will be administered by the HCP. Tr. 92:12-13, 123:13-18, 139:8-10 (Sommi); Tr. 191:2-6 (Berger).

90. Thus, a single entity—an HCP—carries out the three steps of the claimed dosing regimens.

E. Mylan Specifically Intends to Induce Infringement

1. Mylan's Proposed Labels Explicitly Instruct Healthcare Professionals to Infringe the Asserted Claims

91. Mylan's Proposed Labels explicitly instruct HCPs to practice the Asserted Claims. [redacted] PTX-92 at 1; PTX-133 at 1; PTX-162 at 1; PTX-595 at 5; Tr. 120:5-9 (Sommi); Tr. 260:4-9 (Berger) [redacted]

92. [redacted]

[redacted] PTX-92 at 6; PTX-133 at 6; PTX-162 at 6; *see also* PTX-595 at 14. [redacted]. PTX-92 at 7; PTX-133 at 7; PTX-162 at 7; *see also* PTX-595 at 15.

93. [redacted] of the Asserted Claims.

2. Mylan's Proposed Labels Would Inevitably Lead Some Healthcare Providers to Infringe the Asserted Claims

94. The instructions from Mylan's Proposed Labels would inevitably lead some HCPs to perform each step of the claimed dosing regimens and would, therefore, inevitably lead them to infringe the Asserted Claims. Tr. 96:23-97:3, 99:16-21 (Sommi).

95. The evidence was undisputed that missed doses are inevitable—even for patients being treated with PP3M. Tr. 182:21-22 (Berger) (**Q.** Has Trinza solved issues of patient nonadherence? **A.** No. It's still a problem, still a big problem."); Tr. 77:9-11, 107:25-108:1 ("So if this were a perfect world, then you wouldn't have to have a missed dose section."), 119:13-16 (Sommi); Tr. 873:13-874:1, 884:6-7 (Kohler) ("[N]onadherence will occur again."); *see also* PTX-1 at

2:20-24 ("Even with a drug administered once every 3 months . . . , patients at time miss their doses of medication.").

96. In Dr. Berger's own experience, a "large percentage" of patients on Invega Trinza—"more than 50 percent"—have missed a dose of the drug. Tr. 251:1-7 (Berger). And "20 to 30 percent" of Dr. Berger's patients return for an appointment 16 or more weeks after the missed dose. Tr. 251:8-14 (Berger). Dr. Berger acknowledged that some Invega Trinza patients return for reinitiation between 4 and 9 months after their last dose. *See* Tr. 262:4-8, 310:12-18 (Berger). Dr. Kohler similarly testified that he had multiple patients who returned for a reinitiation dose of Invega Trinza between 4 and 9 months after their last dose. Tr. 886:11-14, 888:18-24, 890:1-6 (Kohler). Thus, even though the Invega Trinza label advises that missed doses should be avoided or missed doses occur on exceptional occasions, PTX-43 at 1, 5, patients, including a large percentage of Dr. Berger's patients, still miss doses of PP3M.

97. Some HCPs will inevitably follow the instructions on Mylan's Proposed Labels in treating a patient who was last administered a dose of PP3M four to nine months ago. For example, Dr. Kohler testified that he successfully followed the label instructions to reinitiate Invega Trinza patients who returned 4 to 9 months since their last dose. Tr. 886:11-14, 888:18-24, 890:1-6 (Kohler). Dr. Kohler also testified that it is common for other HCPs to rely on the missed dose

instructions on Invega Trinza's label. Tr. 888:25-889:4 (Kohler). Dr. Kohler's testimony was unrebutted. *See* Tr. 1063:5-8 (Berger); *see also* PTX-220 at 9 (literature showing HCPs typically follow the label instructions for Invega Trinza) ("The vast majority of patients" were initiated onto Invega Trinza "based on the prescribing guidelines.").

98. Dr. Sommi opined that "for most patients," "most" HCPs will "end up following" the missed dose instructions on Mylan's Proposed Labels if a patient presents having had their last PP3M dose 4 to 9 months ago. Tr. 93:18-24 (Sommi). Although Dr. Berger testified that he does not use the missed dose dosing instructions, he concedes patients will show up for treatment and agrees that HCPs will try to follow the instructions on Mylan's Proposed Labels. Tr. 257:21-25 (Berger) (supervising residents who consulted Invega Trinza label when their patients missed PP3M 4-9 months ago); Tr. 264:24-265:4 (Berger) (equating drug label to a speed limit and admitting that he himself follows the speed limit); *see also* Tr. 263:16-19, 263:22-264:2 (Berger). Thus, Mylan's Proposed Labels will inevitably lead some HCPs to reinitiate patients who had their last dose of PP3M 4 to 9 months ago in an infringing manner. Tr. 99:22-25, 103:4-9, 148:4-7 (Sommi).

3. Mylan's Corporate Witness Acknowledged That Mylan Expects Healthcare Providers to Use Its ANDA Products in Accordance with Mylan's Proposed Labels

99. Mylan's 30(b)(6) designee Katie Reed[5] testified that she "would assume [Mylan's customers] are going to use [its product] according to the label that's provided." Reed Dep. Tr. 204:12-24. Reed also testified that "[Mylan] would provide the label with the product to [its] customers and . . . they can use it accordingly." Reed Dep. Tr. 204:12-24. Mylan's Proposed Labels instruct HCPs to use the dosing regimens of the Asserted Claims in an infringing manner. FOF 91-93. Mylan, therefore, specifically intends for HCPs to use its Proposed ANDA Products in a way that infringes the Asserted Claims.

F. Alleged Non-Infringing Uses Do Not Defeat Infringement

100. Mylan contends that its Proposed Labels will not induce infringement because the labels contain instructions for non-infringing uses. Tr. 173:9-20 (Berger). But Mylan failed to show that its Proposed Labels contain non-infringing instructions for the patient population relevant to the Asserted Claims: patients who have "been treated with PP3M," who "had been last administered a PP3M injection 4 to 9 months ago," and for whom the "next scheduled maintenance dose of PP3M should be administered to said patient." PTX-1 at 21:10-16.

[5] Katie Reed is a Director of the North America Portfolio Development team. FPTO, Section VI.A.4.

1. Section 2.6 of Mylan's Proposed Labels

101. [redacted] PTX-92 at 8; PTX-133 at 8 (same); PTX-162 at 8 (same); *see also* PTX-595 at 17. Although he cited these instructions as non-infringing alternatives, Tr. 213:3-7 (Berger), on cross-examination, Dr. Berger conceded that Section 2.6 of Mylan's Proposed Labels is not directed to patients who last received PP3M four to nine months ago. Tr. 276:17-277:1, 281:7-9 (Berger). [redacted] Tr. 276:20-22 (Berger).

2. Section 2.7 of Mylan's Proposed Labels

102. [redacted] PTX-92 at 8; PTX-133 at 8 (same); PTX-162 at 8 (same); *see also* PTX-595 at 17. Again, Dr. Berger relied on these instructions as alleged non-infringing alternatives. Tr. 214:25-215:5 (Berger). And, again, Dr. Berger acknowledged on [redacted] 4. Tr. 279:7-11 (Berger). This does not relate to missed doses of PP3M. Tr. 279:16-17, 282:3-4 (Berger) ("The text does

not say it's about missed doses."). [redacted]

[redacted] PTX-1 at 21:15-16.

VI. MYLAN FAILED TO PROVE THAT THE ASSERTED CLAIMS OF THE 693 PATENT WOULD HAVE BEEN OBVIOUS

103. Mylan failed to prove that any Asserted Claim of the 693 Patent is invalid for obviousness. Mylan's obviousness theories rely on isolated snippets of prior art that are patched together to map onto pieces of the Asserted Claims. But there are wide gaps between the prior art and the claimed inventions, and Mylan's expert, Dr. Forrest, failed to establish that a POSA would have been motivated to bridge these gaps to arrive at the claimed inventions, much less have a reasonable expectation of success in doing so.

A. Dr. Forrest's Obviousness Analysis Was Deficient and Infected with Hindsight

104. Mylan's obviousness case at trial rested on the testimony of its expert, Dr. Forrest. His use of hindsight—forbidden in an obviousness analysis—was blatant and his analysis was fatally deficient.

105. Dr. Forrest was retained by Mylan's counsel in February 2022. Tr. 679:5-9 (Forrest). Just a few weeks after being retained, on March 9, 2022, Dr. Forrest signed a 189-page expert report that included a technical tutorial of paliperidone palmitate, a description of the 693 Patent, an explanation of the 693

Patent's prosecution history, a summary of 15-16 separate references, a detailed basis for his invalidity opinions on obviousness, non-enablement, lack of written description and indefiniteness. Tr. 679:5-680:2 (Forrest). In that time, he also "developed a PK model and ran simulations." Tr. 679:22-680:2 (Forrest).

106. Notably, prior to being retained by Mylan's counsel in this case, Dr. Forrest had never seen the 693 Patent, had never worked with antipsychotics, had no experience with treating psychotic disorders, had never done any work that involved direct patient care, and had no experience with paliperidone. Tr. 676:20-677:11 (Forrest).[6] As Dr. Forrest admitted, Mylan's counsel handed him copies of the references and the specific combinations that he relied on to support obviousness. Tr. 678:14-25 (Forrest). Dr. Forrest simply agreed with counsel. Tr. 678:23-679:3 (Forrest).

107. Dr. Forrest attempted to suggest some virtue to his lack of relevant experience, testifying that it was "in a lot of ways . . . helpful because [his] mind wasn't polluted by art known since 2015." Tr. 475:24-476:1, 677:21-678:10 (Forrest). This did not help his cause. To the contrary, it admitted that Dr. Forrest

[6] On March 31, 2022—about three weeks after the 189-page expert report was served in this case—Dr. Forrest submitted another expert report on invalidity of two separate patents in a different patent litigation on a different drug involving a completely different disease, *i.e.*, heart failure. Tr. 680:8-681:12 (Forrest). Remarkably, Dr. Forrest was employed by the University of Kansas with full-time teaching responsibilities while preparing these two expert reports. Tr. 681:13-18 (Forrest).

lacked the requisite expertise to reach his own independent opinions in the short time between when he was retained and when he signed his report for this case. Dr. Forrest simply relied on the hindsight-driven analysis that Mylan's counsel fed him.

1. Mylan's Prior Art References Lack Key Elements of the Asserted Claimed

108. The only obviousness combination Dr. Forrest presented at trial relies on seven primary references consisting of three PP3M references (JAMA, NCT 423, and the 2014 Press Release) and four PP1M references (Invega Sustenna Label, the 536 Publication, the 519 Publication and Samtani 2009). Tr. 683:12-684:2 (Forrest). Even when combined, Dr. Forrest admitted that key elements of the Asserted Claims were absent from the prior art.

109. Dr. Forrest admitted that he did not identify any prior art reference as disclosing (a) "a missed dose regimen for PP3M," Tr. 684:18-20 (Forrest); (b) "the 4-9 month target patient population," Tr. 685:9-12 (Forrest); (c) "using PP1M after a patient had been advanced to PP3M," Tr. 685:13-16 (Forrest); or (d) "using PP3M without first stabilizing the patient on PP1M for at least a few months," Tr. 686:2-14 (Forrest). *See also* Tr. 598:3-15 (Sommi). Dr. Forrest's admissions, and the unscientific and inconsistent application of his various theories, are fatal to Mylan's attempt to prove obviousness.[7]

[7] To the extent the dosing regimens of the Asserted Claims require seven steps as Dr. Berger asserted, Dr. Forrest failed to provide an obviousness analysis under

a. JAMA (PTX-113)

110. JAMA is titled, "Efficacy and Safety of the 3-Month Formulation of Paliperidone Palmitate vs Placebo for Relapse Prevention of Schizophrenia: A Randomized Clinical Trial." PTX-113 at 1; Tr. 541:25-542:2 (Sommi).

111. In this study, all patients were administered PP1M during a 17-week transition phase. Tr. 542:3-9, 645:18-21 (Sommi). Patients stabilized on PP1M (*i.e.*, patients "on the same dose at least two or three times" and "psychiatrically stable" based on clinical assessment using a PANSS score) received one dose of PP3M, and three months later entered the double-blind phase during which patients were randomized to receive either PP3M or placebo (*i.e.*, no antipsychotic medicine). Tr. 694:18-695:1 (Forrest); Tr. 542:10-543:12, 631:22-632:6 (Sommi). Patients not stabilized on PP1M were not eligible to enter the double-blind phase and could not receive PP3M. Tr. 543:8-10 (Sommi).

112. JAMA includes a table that sets forth the "corresponding dose of PP3M" for each "specific dose of PP1M" on which the patient had been stabilized. Tr. 540:3-13 (Sommi); PTX-113 at 68. These doses were used for the "***initial***

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that claim construction or attempt to identify all seven steps in the prior art, including, purported step 1 of missing a dose, purported step 2 of returning for treatment between four to nine months since the last injection, purported step 4 of returning for treatment on about the fourth day through the 12th day after first re-initiation loading dose, and purported step 6 of returning for treatment on the 23rd to 37th day after the first re-initiation loading dose. Tr. 291:9-15, 292:8-13, 292:17-20, 292:24-293:2 (Berger); Tr. 771:21-772:22 (Forrest).

conversion from PP1M to PP3M," in an "initiation regimen" using PP1M for advancing to PP3M. Tr. 540:3-13 (Sommi); Tr. 694:15-17 (Forrest). But JAMA's table of doses does not teach or suggest using PP1M ***after*** a patient had been advanced to PP3M. Tr. 540:14-17 (Sommi); *see also* Tr. 685:13-16 (Forrest).

113. Although JAMA provides limited average plasma concentration information for PP3M, Dr. Forrest admitted it is "incomplete" and did not rely on it. Tr. 509:11-14 (Forrest). JAMA measured efficacy as time to relapse from randomization and would not have enabled a POSA to predict efficacy based on plasma concentrations of paliperidone. Tr. 543:23-25 (Sommi).

b. The 2014 Press Release

114. The 2014 Press Release, is titled "Janssen Investigational Treatment for Schizophrenia Shows Positive Efficacy, Delays Relapse." PTX-160 at 1. "It [is] a press release about the JAMA study" reporting that the study was "stopped because . . . it was a positive study." Tr. 553:5-8 (Sommi). Consistent with JAMA, the 2014 Press Release confirms that "the study subjects were first ***stabilized*** on Sustenna" (*i.e.*, PP1M) before advancing to PP3M. Tr. 553:10-15 (Sommi). The 2014 Press Release adds nothing to JAMA. Tr. 553:16-18 (Sommi).

c. NCT 423 (PTX-158)

115. The final PP3M reference, NCT 423, is a simplified summary of a clinical trial protocol found at clinicaltrials.gov, titled "Study of Paliperidone

Palmitate 3 Month and 1 Month Formulations for the Treatment of Patients With Schizophrenia." PTX-158 at 1; Tr. 540:25-541:4 (Sommi). "The purpose of this study is to demonstrate that [PP3M] is as effective as [PP1M] in the treatment of patients with schizophrenia ***who have been stabilized on PP1M***." PTX-158 at 4. NCT 423 does not contain any results. Tr. 541:22-23 (Sommi).

116. NCT 423 describes that all patients were to be given PP1M for a 17-week transition phase and, "if they were ***clinically stable*** on PP1M, they were randomly assigned to either stay on PP1M or switch to PP3M." Tr. 541:11-18 (Sommi); *see also* Tr. 450:7-10 (Forrest). Without stabilization on PP1M, patients were not eligible to receive PP3M. Tr. 541:19-21 (Sommi).

117. NCT 423 provides dosages of "PP3M, when you are moving from PP1M to PP3M" after being stabilized on PP1M, Tr. 539:20-540:2 (Sommi); PTX-158 at 5, but it does not teach or suggest returning to PP1M after a patient had been advanced to PP3M, Tr. 540:14-17 (Sommi).

d. Differences Between the PP3M Prior Art and the Asserted Claims

118. The PP3M references lack key elements of the Asserted Claims. None of the PP3M prior art references (a) "disclose[] a missed dose regimen for PP3M," (b) "help you identify the four-to-nine-month population," (c) taught "going back to PP1M after you advanced a patient to PP3M," or (d) taught

"something other than stabilizing a patient on four or more doses of PP1M before advancing them to PP3M." Tr. 554:4-11 (Sommi).

2. Dr. Forrest's Reliance on PP1M References Was Hindsight-Driven and Scientifically Invalid

119. In an attempt to fill some of the gaps in the PP3M prior art disclosures, Dr. Forrest relied on four PP1M references—the Invega Sustenna Label, the 536 Publication,[8] the 519 Publication,[9] and Samtani 2009.

120. None of the PP1M references suggest the key elements missing from the PP3M prior art. Tr. 554:15-555:10 (Sommi). For example, Dr. Forrest did not opine that the PP1M prior art provided any reason for a POSA either to give a patient a dose of PP3M before they had been clinically stabilized on PP1M for several months, or to administer different formulations of LAIs in a missed dose

[8] The 536 Publication (US 2011/0105536) is a published application titled "Dosing Regimen Associated with Long-Acting Injectable Paliperidone Esters." PTX-116 at 1. It taught that simulating missed dose scenarios using PK models could be used to design missed dose regimens for PP1M. PTX-116 ¶ [0088]; *see also* Figs. 2 and 3. It does not disclose PP3M dosing regimens. Tr. 435:25-436:2 (Forrest). Dr. Forrest admitted that his primary reliance on the 536 Publication is cumulative to that of the Invega Sustenna Label where he cites to the same reinitiation instructions for ***PP1M*** patients who last received PP1M between 6 weeks to 6 months ago. Tr. 413:3-12 (Forrest).

[9] The 519 Publication is a patent application publication of US 2009/0163519, titled "Dosing Regimen Associated with Long-Acting Injectable Paliperidone Esters." PTX-115 at 1. It is about PP1M. Tr. 414:16-21 (Forrest). Dr. Forrest admitted that his primary reliance on the 519 Publication is cumulative to that of the 536 Publication and the Invega Sustenna Label. Tr. 413:3-12 (Forrest).

regimen such that a patient was returned to PP1M after having been advanced to PP3M (as in the claimed dosing regimen).

121. Dr. Forrest relied on portions of the PP1M prior art only to opine that a POSA would have been motivated to develop a missed dose regimen for PP3M and to support his opinion that identifying the 4-9 month target clinical situation for a PP3M intermediate missed dose regimen would have been obvious. Tr. 586:6-588:8 (Sommi). But to do so, Dr. Forrest cherry-picked from the references in a biased manner, ignoring the teachings of the prior art when they led away from the claimed invention. His hindsight-driven approach lacks scientific credibility and cannot sustain a conclusion of obviousness.

a. Invega Sustenna Label Extrapolation Theory for the Intermediate Window

122. First, Dr. Forrest relied on an extrapolation from the Invega Sustenna Label (PTX-106) to estimate the front end of the intermediate window for a PP3M missed dose regimen. Notably, the label addresses only missed dose instructions for PP1M and does not mention PP3M or any PP3M missed dose instructions. Tr. 704:13-20 (Forrest); Tr. 554:15-20 (Sommi).

123. Referring to Section 2.3 titled "Missed Doses," and in particular, the intermediate window of PP1M patients at "[m]ore than 6 weeks to 6 months since last injection" (PTX-106 at 4-6; Tr. 705:2-5 (Forrest)), Dr. Forrest noted that the front end of the Invega Sustenna intermediate window started at six weeks, or about

1.4 times the one-month dosing interval of PP1M (30 days). Tr. 707:12-18 (Forrest); Tr. 558:9-10 (Sommi).

124. Dr. Forrest then applied this multiplier (1.4x) to the three-month dosing interval of PP3M (90 days), and calculated 4.2 months (126 days) as the front end of the intermediate missed dose window for PP3M. Tr. 707:12-18 (Forrest); Tr. 558:9-14 (Sommi). Dr. Forrest concluded that 4.2 months was close enough to the 4-month mark recited in the 693 Patent claims. Tr. 707:23-708:2 (Forrest).

125. In a transparently results-oriented maneuver, Dr. Forrest disavowed using the same approach to calculate the back end of the intermediate window for PP3M. That is because, as Dr. Forrest admitted, if the same logic were applied to the back end, a POSA would calculate the back end at 18 months. Tr. 710:13-25 (Forrest); *see also* Tr. 558:20-559:7 (Sommi) (back end of intermediate window for PP1M is 6 months, *i.e.*, six times the dosing interval; multiplying the PP3M dosing interval by six would lead to 18 months). Using the same theory would set the back of the intermediate window at 18 months, "about twice as long" as the 9-month back end recited in the Asserted Claims. Tr. 559:10-13 (Sommi).

126. Dr. Forrest had no credible explanation as to why he did not use the same approach to extrapolate both the front and back end of the intermediate window. When confronted on cross-examination with this scientific inconsistency,

Dr. Forrest was evasive, overly defensive, and ultimately impeached by his own deposition testimony. *See* Tr. 709:16-711:20 (Forrest) ("**Q.** Well, applying your own logic then, you would calculate the back end of the intermediate window for PP3M to be 18 months, right?" **A.** . . . Let me say no, that I would need to explain further."; "**Q.** At your deposition, . . . I asked you the question, 'And if you applied it to the back end, you would get to about 18 months, or about 540 days.' You said yeah. You're relying that, of course, as I discussed in my report, would see there it would be potentially that long. Right? **A.** Yes.").

127. As Drs. Sommi and Gobburu explained, a POSA would not have embarked down the road of extrapolating information about PP3M from the Invega Sustenna Label, much less have done so with a reasonable expectation of success. *See* Tr. 558:15-19 (Sommi); Tr. 813:9-12, 814:16-19 (Gobburu). But if a POSA were to use Dr. Forrest's extrapolation, at a minimum the POSA would have applied it uniformly and consistently, not selectively as Dr. Forrest did, to extrapolate both the front and back end of the intermediate window using the same logic. Tr. 559:19-560:1 (Sommi). Dr. Forrest's inconsistent and scientifically indefensible approach undermined the credibility of his obviousness analysis, instead confirming that it was a hindsight-driven effort to arrive at the Asserted Claims rather than a legitimate effort to describe what would have been obvious to a POSA at the effecting filing date of the 693 Patent.

b. 4-5 Half-Life Extrapolation Theory

128. Unable to extrapolate from the Invega Sustenna Label to a 9-month back end for the PP3M missed dose intermediate window, Dr. Forrest pivoted to a completely different theory, based on drug half-life. Tr. 711:22-25 (Forrest). The premise of this theory, relying on the 536 Publication (PTX-116 ¶ [0103]), is that it takes about 4-5 half-lives for a drug to be completely eliminated from the systemic circulation which, in Dr. Forrest's opinion, would signify what the back end of the intermediate window should be because that is when drug has been essentially eliminated from the patient's blood stream. Tr. 712:2-9 (Forrest); Tr. 560:2-21 (Sommi).

129. A POSA would not have relied on a 4-5 half-life theory, or any theory based on half-life to identify only one end of the window. Tr. 559:19-560:1, 586:18-24 (Sommi). But if they did, to apply the 4-5 half-life theory to PP3M, a POSA would have needed to know the half-life of PP3M. Tr. 712:12-14 (Forrest); Tr. 560:22-24 (Sommi). But as Dr. Forrest admitted, the half-life of PP3M was not known in the prior art. Tr. 712:25-713:3 (Forrest); Tr. 560:25-561:3 (Sommi).

130. So Dr. Forrest assumed the half-life of PP3M could be divined from the dosing interval of PP3M. That is a scientifically erroneous assumption.[10] Not

[10] As it turns out, the actual measured half-life of PP3M (reported after the 693 Patent's filing date) is approximately 120 to 140 days (*i.e.*, approximately 4-4.5 months). PTX-192 at 6; Tr. 817:24-818:6, 861:8-14 (Gobburu).

even Mylan agrees with this assumption. *See, e.g.*, Shaw Dep. Tr. 136:9-12 ("[W]ithout measuring the blood levels, you cannot predict what the half-life of Mylan's proposed PP3M is."). Dr. Forrest first assumed that the half-life for PP1M was 30 days (based on its dosing interval), and then multiplied that by three to assume a half-life for PP3M of 90 days. Tr. 713:17-20, 717:21-23 (Forrest).

131. But PP1M's measured half-life was disclosed in the 519 Publication. It taught that the half-life of PP1M was "dose-related," Tr. 562:21-25 (Sommi), increasing "from 25 days (median) after the 25 mg eq. dose to 40-49 days (median) after the 100 and 150 mg eq. dose, for both injection sites." PTX-115 ¶ [0098]; *see* Tr. 713:14-16 (Forrest). In assuming the half-life of PP1M was uniformly 30 days, Dr. Forrest ignored the reported, dose-dependent half-life of PP1M. Tr. 563:1-7 (Sommi). A POSA would have known this assumption to be scientifically unreasonable, and instead "would have used the actual data." Tr. 563:11-22 (Sommi).

132. Attempting to justify his 30-day half-life assumption for PP1M, Dr. Forrest relied on an observation in the 536 Publication that "[t]he results in Table 3 showed that, for all depot antipsychotics, the administration interval was in the range of about 1-2 half-life for each product." PTX-116 ¶ [0103]; Tr. 714:1-5 (Forrest). There are several scientific flaws with this.

133. First, it ignores the ***actual*** half-life reported for PP1M is not 30 days. Tr. 717:11-13 (Forrest); PTX-115 ¶ [0098]. A POSA would not rely on an estimate when actual data were available. Tr. 563:11-22 (Sommi). As Dr. Forrest himself volunteered, a POSA would "use all the data you had at hand," Tr. 720:1 (Forrest).

134. Second, even if a POSA were to use the 536 Publication's statement to estimate a half-life for PP1M, it would teach that the 30-day dosing interval for PP1M would be 1-2 half lives, meaning that one half-life would be anywhere from 15 to 30 days for PP1M. Tr. 717:6-10 (Forrest); Tr. 561:9-19 (Sommi).[11]

135. Third, the observation reported in the 536 Publication was expressly not about paliperidone palmitate, a fact that Dr. Forrest purposely tried to obfuscate, if not intentionally misrepresent at trial. FOF 211. Specifically, the 536 Publication's statement is based on "a literature search [that] was conducted to evaluate the pharmacokinetic characteristics of ***other*** long acting injectable antipsychotics." PTX-116 ¶ [0102]. The "authors made an observation that there was a relationship between the administration interval and the half-life" for the products listed in Table 3. Tr. 561:11-14 (Sommi).

136. But Table 3 does ***not*** include paliperidone palmitate. Dr. Forrest chose not to show Table 3 to the Court in his direct examination. Tr. 715:11-15,

[11] Again, this is inconsistent with the actual half-life of PP1M as reported to be as low as 25 (not 15) days and also up to 49 (not 30) days. Tr. 717:11-13 (Forrest).

715:25-716:2 (Forrest); Tr. 561:25-562:1 (Sommi). Instead, he testified that the 536 Publication was "all about paliperidone palmitate." Tr. 430:4-6 (Forrest). On cross-examination, Dr. Forrest could muster no credible explanation for omitting Table 3 from his direct testimony. *See* Tr. 713:23-715:10 (Forrest).

137. Dr. Forrest then multiplied the purported 30-day half-life of PP1M by 3 and assumed the half-life of PP3M would be about 90 days. Tr. 717:21-23 (Forrest); Tr. 561:9-19 (Sommi). Dr. Forrest then applied his 4-5 half-life theory to calculate the back end of the intermediate window for PP3M to be at about 12-18 months. Tr. 464:24-465:6 (Forrest); Tr. 564:8-15 (Sommi).

138. Again, because he was using impermissible hindsight, Dr. Forrest knew that this was not the answer he needed, so he had to rely on something else to get to the 9-month target in the Asserted Claims. Tr. 564:25-565:7 (Sommi).

139. Prior to trial, Dr. Forrest relied on a PK modeling exercise allegedly to identify the back end of the intermediate missed dose window for PP3M as 9 months. Tr. 720:2-6 (Forrest). At trial, however, Dr. Forrest unveiled a new, previously undisclosed theory, testifying that a POSA could have used JAMA to arrive at the 9-month target and that his PK modeling was only used to validate the conclusion reached under this new theory. Tr. 509:2-4 (Forrest).

3. Extrapolation from JAMA

140. The premise of Dr. Forrest's new JAMA theory is that a POSA would look at the Kaplan-Meier plot of Figure 2A (showing data from an interim analysis) and—notwithstanding the author's express conclusion that the plot shows the median time to relapse was 274 days after randomization (*i.e.*, 12 months since the last PP3M injection)—a POSA would somehow eyeball the graph, make a "natural jump" backwards, and choose 180 days after randomization (*i.e.*, 9 months since the last PP3M injection) to identify the back end of the intermediate window. Tr. 465:14-468:22 (Forrest). Dr. Forrest's testimony on this was not credible.

a. A POSA Would Not Disregard a Final Analysis and Rely on Interim Analysis

141. To rely on Dr. Forrest's JAMA theory, a POSA would have to rely on the interim analysis and ***ignore*** the additional data collected and reported as part of JAMA's final analysis. As Dr. Forrest admitted, this more complete data set showed that the time to relapse was ***395*** days after randomization (around 16 months since the last PP3M injection). Tr. 703:24-704:4 (Forrest); Tr. 549:9-11 (Sommi); PTX-113 at 4.[12] Dr. Forrest's *ipse dixit* testimony that "JAMA told us to ignore [the final analysis] data" is not credible. Tr. 720:13-17 (Forrest).

[12] Based on an analysis of all data collected, JAMA discloses that "the estimated median time to relapse for patient switched to placebo after stabilization on various formulations of paliperidone show that [PP3M] has a longer time to relapse

142. Indeed, Dr. Forrest later contradicted his own suggestion that a POSA would ignore data in JAMA. Struggling to defend the inconsistent application of his various theories to arrive at the intermediate window, Dr. Forrest stressed on cross-examination—several times—that a POSA would "use all the data you had at hand." Tr. 720:1; Tr. 720:10-12 (Forrest) ("You would put the appropriate weight on each one and understand which is most relevant, ***but you would use data that is available***."). Confronted with the contradiction, Dr. Forrest was unable to find a credible explanation for why a POSA would use all the data in the prior art, yet ignore the final analysis from JAMA. Tr. 720:13-721:13 (Forrest).

143. In fact, a POSA would not disregard that additional data included in the final analysis in JAMA. Tr. 547:17-19 (Sommi). The interim analysis was conducted because JAMA was a relapse prevention trial involving patients with schizophrenia who received placebo; "there's a risk of relapse," and therefore "from an ethical point of view, you take a peek at the data at the prescribed time," here after 42 relapses. Tr. 546:4-16 (Sommi). At that point, the "committee gets together, they do the analysis, they make a decision . . . if the study is positive." Tr. 546:23-547:6 (Sommi). The analysis conducted at this time, to determine whether to unblind the study early, is the interim analysis. Tr. 546:23-547:6 (Sommi). But

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compared with the estimates with [PP1M] and oral extended-release paliperidone (395 vs 172 and 58 days, respectively)." PTX-113 at 7.

"[w]hen they say the study is over, it may take three, four, five, six months to get all the patients out of the study safely," during which they are "still collecting data." Tr. 547:11-16 (Sommi); PTX-113 at 3 ("Results through the end of the DB phase after early termination of the study (*i.e.*, cumulative data including those from before the interim cutoff data) are reported herein as the final analysis . . . ."). A POSA would have had no reason to ignore the final analysis.

b. A POSA Would Not Rely on JAMA for Setting a Missed Dose Window

144. The second leap of faith required by Dr. Forrest's JAMA theory is accepting that a POSA would rely on the outcome measures for this study in setting a window for an intermediate missed dose regimen. This is not credible.

145. JAMA's interim (and final) analyses were based on measuring delay of time to relapse, meaning becoming hospitalized or experiencing a significant increase in PANNS score. Tr. 543:13-22 (Sommi); Tr. 692:6-11 (Forrest). Notably, these were not pharmacokinetic outcomes; they were clinically defined. Tr. 543:23-25 (Sommi). But Dr. Forrest lacks the expertise to opine on clinical considerations, as he admitted that he has not done any research with antipsychotics and he is not a clinician. Tr. 676:23-677:4, 1191:1-2 (Forrest).

146. In contrast, Janssen's expert, Dr. Sommi, is a Board-certified psychiatric pharmacist with extensive experience caring for, and teaching about the care of, psychiatric patients. Tr. 46:1-50:2 (Sommi). He has served many times as

an investigator in placebo-controlled clinical trials, Tr. 50:3-51:24 (Sommi), and in so doing has dealt with interim analyses for such studies, Tr. 547:10-11 (Sommi).

147. Dr. Sommi testified credibly that a POSA would not have adopted Dr. Forrest's approach of extrapolating the intermediate window for a missed dose regimen from the relapse data reported in JAMA. Tr. 545:11-14 (Sommi). But if a POSA were to attempt to make some conclusions from these data, the POSA certainly would not have ignored the data from the ***final*** analysis establishing that the median time to relapse for the placebo group was 395 days after randomization. PTX-113 at 4; Tr. 545:25-546:3, 548:16-549:14 (Sommi).

c. Dr. Forrest's Hindsight-Driven Change in Positions

148. Even if it was plausible to accept Dr. Forrest's incorrect opinion that a POSA would ignore the final analysis and focus instead on the interim analysis of JAMA, that would still not lead a POSA to identify the 9-month back end of the intermediate dosing window for PP3M.

149. JAMA reports that the median time to relapse at the interim analysis was 274 days since randomization. Tr. 549:6-9 (Sommi); Tr. 696:13-20 (Forrest). Apparently having forgotten that all patients had been given a dose of PP3M three months ***before*** being randomized, at his deposition, Dr. Forrest latched onto the median time to relapse of 274 days (9 months after randomization) as directly teaching the 9-month back end of the intermediate window. Tr. 550:18-20

(Sommi). That was a mistake; 274 days from randomization is actually 12 months since the last PP3M injection.[13]

150. Reflecting his relentless and hindsight-driven quest to arrive at the Asserted Claims, Dr. Forrest responded to this error by changing his opinion. For the first time, at trial, Dr. Forrest identified an earlier time point (180 days) based on his interpretation of Figure 2A, testifying that it is a "natural jump" to get from 274 days to 180 days. Tr. 467:25-468:2 (Forrest). Dr. Forrest offered no cogent explanation why a POSA would make this "natural jump" to the 180-day number, rather than relying on the 274-day number he relied on at deposition (or the 395-day number from the final analysis that he ignored). *See* Tr. 697:19-698:8 (Forrest). Nor did Dr. Forrest explain why he had not identified this supposedly "natural jump" at his deposition, when he mistakenly believed he could have arrived at his desired result without a "natural jump." *See* Tr. 698:9-701:20 (Forrest); FOF 210.

[13] This time was measured from the time that the patients were randomized into two groups: one receiving a placebo and the other continuing on PP3M. Tr. 548:16-549:3 (Sommi); *see also* Sommi Validity Demonstratives Slide 20. But all patients received PP3M three months prior to when they were randomized. Tr. 549:4-5 (Sommi). So, in terms of the time since their last dose of PP3M, at the interim analysis, the median time to relapse for the placebo group was 274 days (9 months) since they were randomized—or about 12 months since the last PP3M injection. Tr. 549:6-9 (Sommi); Tr. 696:13-20 (Forrest); *see also* Sommi Validity Demonstratives Slide 20.

d. Dr. Forrest's Selective Application of His JAMA Theory

151. As he did with his other theories, Dr. Forrest selectively applied his JAMA theory; he used it only to identify the back end of the intermediate window, but not the front. Tr. 552:7-553:1, 587:7-9 (Sommi). A POSA would not have used JAMA to identify the 4-9 month clinical situation. *See* Tr. 545:11-14, 649:18-20 (Sommi). But, assuming a POSA were to adopt Dr. Forrest's approach, they would have identified about 6 months as the front end of the intermediate window. Tr. 552:7-553:1 (Sommi). Dr. Forrest made no attempt to do this analysis, Tr. 550:25-551:2 (Sommi), further evidence that his analysis lacks credibility.

4. Dr. Forrest's Flawed PK Modeling and Extrapolations

152. Unable to identify the 9-month mark for the back end of the intermediate window through his other extrapolation theories, Dr. Forrest purportedly developed a simple PK model and ran simulations exclusively for this purpose (at least that was his testimony before trial). Tr. 480:1-4 (Forrest); Tr. 587:10-13 (Sommi). Dr. Forrest relied on Samtani 2009[14] to build PP1M and PP3M PK models, and used those to perform simple calculations in an Excel spreadsheet. Tr. 502:18-23, 722:11-13 (Forrest). Notably, Samtani 2009 does not

[14] Samtani 2009 is titled "Population Pharmacokinetics of Intramuscular Paliperidone Palmitate in Patients with Schizophrenia: A Novel Once-Monthly, Long-Acting Formulation of an Atypical Antipsychotic." PTX-118 at 1; Tr. 843:11-19 (Gobburu).

mention PP3M, let alone report any PP3M data. Tr. 724:16-18 (Forrest); Tr. 820:24-25 (Gobburu). And Dr. Forrest's analysis was riddled with errors and inconsistencies.

153. Samtani 2009 "describes the population pharmacokinetic modeling of PP1M formulation." Tr. 820:20-23 (Gobburu). Samtani 2009 discloses that a PP1M model was developed through a rigorous pop-PK analysis, based on, and validated with, close to 16,000 pharmacokinetics samples from about 1,400 patients who received PP1M. Tr. 566:21-25 (Sommi); Tr. 724:19-22 (Forrest). From this, a POSA would have understood that a PK model for PP3M could not be built without actual data relating to the PK of PP3M. Tr. 567:12-15 (Sommi).

154. But such PP3M data was not in the prior art. So the model Dr. Forrest developed and presented to the Court was created by extrapolating from information about PP1M in Samtani 2009. Tr. 723:23-724:1 (Forrest). Dr. Forrest tried to dismiss the lack of a pop-PK analysis for PP3M as unnecessary, testifying it is "essentially overkill to go back and design—and perform an entire population PK study" for PP3M. Tr. 515:5-7 (Forrest). But that is not scientifically credible.

155. Consider the Janssen scientists working on the PP3M project; even with all the data and modeling they had in hand for PP1M—including all the unpublished individual patient-level data underlying the model reported in Samtani 2009—they nevertheless developed a separate "comprehensive population

pharmacokinetics (PK) model" for PP3M using 8,990 PK samples from 651 patients. PTX-1 at 17:25-35; Tr. 811:23-812:9 (Gobburu). That model allowed the inventors to accurately predict plasma concentrations and develop the claimed reinitiation dosing regimens. *See* PTX-1 at 17:45-46, 17:56-58, 19:56-58, Figs. 4A-4C. Without PP3M clinical data, a POSA could not have developed a pop-PK model for PP3M and would not have arrived at the claimed reinitiation dosing regimen for PP3M. Tr. 811:12-15, 812:10-12 (Gobburu).

a. Dr. Forrest's Model Ignored Important Parameters Reported to Influence PK of Paliperidone Palmitate

156. A POSA would not have built a PP3M PK model using PP1M data gleaned from Samtani 2009, nor would they have used the model to simulate dosing scenarios for PP3M. Tr. 573:11-18 (Sommi); Tr. 813:10-12, 814:16-815:1 (Gobburu). But if a POSA were to attempt to do so, at a minimum, a POSA would have utilized ***all*** of the parameters Samtani 2009 reported to influence the PK of paliperidone palmitate, and not cherry-picked some while ignoring others, as Dr. Forrest did. Tr. 813:13-16, 821:20-822:11 (Gobburu). Dr. Forrest, again, contradicted his own testament that "[y]ou use all the data you had at hand," Tr. 720:1 (Forrest), by not utilizing "the full known characteristics of PP1M." Tr. 820:8-10 (Gobburu).

157. Samtani 2009 taught that "antipsychotics are rife with inter-patient and intra-patient variability, so the pop-PK takes lots of different factors into

account." Tr. 567:21-25 (Sommi). Table III in Samtani 2009 identified 25 such parameters that were used for describing and predicting the PK of PP1M using a model. Tr. 725:2-6 (Forrest); Tr. 821:6-11 (Gobburu).

158. Among the parameters that were identified, Samtani 2009 concluded that the PK properties of paliperidone palmitate are mostly influenced by BMI (body mass index), CLCR (creatinine clearance), INJS (injection site), IVOL (injection volume), and NDLL (needle length). Tr. 725:7-14 (Forrest); Tr. 568:9-22 (Sommi); PTX-118 at 1. Some of these and other parameters in Table III account for the "variability between patients" that pervades pharmacology. Tr. 822:3-11 (Gobburu); *see also* Tr. 807:17-808:15 (Gobburu); PTX-145 at 491 ("Substantial differences in response to drugs commonly exist among patients.").

159. Dr. Forrest agrees that a POSA would have understood that patients have variability in their response to drugs. Tr. 724:23-725:1 (Forrest). Yet, Dr. Forrest chose to use only ***4*** out of the 25 parameters from Table III—CL (clearance), V_d (volume of distribution), K_a shift factor for deltoid injection, and the K_a (absorption rate constant). Tr. 725:15-25 (Forrest); Tr. 569:10-15 (Sommi). None of these address interpatient variability; he ignored "the variability between patients" where "the range of the blood levels . . . is dictated by whether the patient is a female or is a male . . . [or] is obese or nonobese." Tr. 822:3-11 (Gobburu).

160. Dr. Forrest's attempt to downplay his omissions were not credible. He testified that, because factors such as BMI or age did not affect the actual reinitiation instructions in the Invega Sustenna Label, he did not need to account for them in his PP3M model. Tr. 505:3-24 (Forrest). But as Dr. Gobburu credibly explained, "population PK modeling, which describes both the average as well as the variability between patients, including these risk factors . . . would be used to derive those dosing instructions in the first place." Tr. 822:12-21, 823:18-824:2 (Gobburu). The fact that the final instructions were not dependent on age or BMI is irrelevant to what a POSA would have done to develop those instructions.

b. Dr. Forrest's Model Ignored PP1M's Complex Absorption

161. Dr. Forrest's model also ignored the known complexities of PP1M absorption. As Dr. Gobburu explained, Samtani 2009 "reported that the PP1M absorption is rather more complex than the simplified [model] that was used by Dr. Forrest." Tr. 821:20-822:2 (Gobburu). Samtani 2009 teaches that "a dual absorption pharmacokinetic model best described the complex pharmacokinetics of [PP1M]." PTX-118 at 1; Tr. 570:9-12 (Sommi). This reflects the "biphasic" absorption of PP1M. Tr. 727:19-21 (Forrest); Tr. 570:9-16 (Sommi).

162. Dr. Forrest acknowledges that a biphasic absorption process has an initial zero-order component, Tr. 727:22-24 (Forrest), through which "a fraction of the dose f_2 is absorbed relatively quickly." PTX-118 at 1; Tr. 728:4-6 (Forrest).

"[T]he zero order process really talks about where the concentration goes up really quickly. That's a burst of concentration." Tr. 570:17-22 (Sommi). Following the zero-order process, there is a first-order process that "allows that drug to be given over a longer period of time." Tr. 570:23-571:6 (Sommi).

163. Dr. Forrest admitted that, like PP1M, "the absorption of PP3M could also be divided biphasically." Tr. 728:10-13 (Forrest). But Dr. Forrest ignored this in his models, choosing to use only a simple first-order equation for both PP1M and PP3M. Tr. 728:14-17 (Forrest); Tr. 571:13-15 (Sommi).

164. Trying to excuse this lapse, Dr. Forrest suggested that his "model wasn't built to determine the early phase with high precision," Tr. 742:17-743:3 (Forrest), stating that he "only car[ed] about [his] model accurately simulating the elimination phase," Tr. 742:23-24; Tr. 784:16-19 (Forrest) ("I wasn't trying to count from the very beginning because that's not very important for re-dosing").

165. According to Dr. Forrest, he did not need to include a zero-order absorption "because that was such a minor component." Tr. 514:19-21 (Forrest); Tr. 729:3-10 (Forrest) ("Yes, 17%"). But, as Dr. Sommi credibly explained, a POSA would have understood that 17% of the drug being absorbed through the zero-order initial burst is "about somewhere between the fifth and the sixth of the dose, so it's a pretty ***significant*** amount." Tr. 571:7-12 (Sommi). The goal of pharmacokinetics is to account all aspects of a PK profile: "how fast it raises, how

long it stays in the sweet spot . . . and how fast or slow it goes out of the body." Tr. 826:25-827:10 (Gobburu). A POSA would have found Dr. Forrest's approach to be "unscientific" because he focuses only on "a sliver of time window and ignor[es] the rest." Tr. 827:11-15 (Gobburu).

c. Dr. Forrest's Assumptions Cannot Be Reconciled

166. For his model to work, Dr. Forrest needed an absorption rate constant ("K_a") for PP3M that could be plugged into his simple first order equation. Tr. 735:15-18 (Forrest). But the K_a for PP3M was not known in the prior art. Tr. 574:10-14 (Sommi); Tr. 815:2-7 (Gobburu). So, Dr. Forrest extrapolated the K_a of PP1M from Samtani 2009's PP1M model and simply divided it by three. Tr. 735:19-736:5 (Forrest); Tr. 574:15-20 (Sommi); Tr. 815:17-18 (Gobburu).

167. Dr. Forrest's extrapolation was not reasonable because the K_a Samtani 2009 reported was based on a pop-PK model that accounted for biphasic absorption; it could not be plugged into a simple first-order model. Tr. 573:15-22, 574:21-575:1 (Sommi). A POSA would have known that "the pharmacokinetics of PP1M at least were rather complicated and complex and very different from what we had up until that point in the market. So applying simple math [as Dr. Forrest did] probably wasn't going to work." Tr. 555:16-22 (Sommi).

168. Dr. Gobburu—a renowned pharmacometrician with 12 years of FDA experience, including time as the founding director of the Division of

Pharmacometrics—also found this to be "unscientific." Tr. 802:23-804:7, 813:9-12 (Gobburu). "The use of [PP1M] data to extrapolate to [PP3M] data is not based on science." Tr. 813:10-12 (Gobburu). "If you change the formulation" from PP1M to PP3M, you "cannot predict the pharmacokinetics of the new formulation." Tr. 848:15-19 (Gobburu).[15] As a result, a POSA would not have had a reasonable expectation of success in following Dr. Forrest's approach and extrapolating the absorption characteristics of PP3M from data about PP1M. Tr. 815:5-20 (Gobburu); Tr. 555:25-556:4 (Sommi).

169. But Dr. Forrest simply assumed that if PP3M lasts three times longer than PP1M, "then it should be one-third slower to ensure that the drug is oozing out of the muscle for three months." Tr. 815:8-14 (Gobburu). Based on this assumption, Dr. Forrest divided the absorption rate constant of PP1M by three. Tr. 815:17-18 (Gobburu). This was "a naïve oversimplification, unscientific approximation" that a POSA would not have made. Tr. 815:8-20 (Gobburu).

170. Assuming *arguendo* that a POSA would have followed such an unscientific approach, a POSA would have at least checked the conclusions against known data to confirm whether the approach was valid. Tr. 576:3-4 (Sommi). One way to do so would have been to calculate the half-life from the extrapolated

[15] Likewise, Mylan's 30(b)(6) witness, Dr. Andrew Shaw, testified that "without measuring the blood level, you wouldn't know in any way . . . what Mylan's proposed PP3M PK profile would look like." Shaw Dep. Tr. at 136:4-8.

absorption rate constant. Tr. 575:20-576:9 (Sommi). Dr. Forrest testified about a simple equation for doing so: "the half-life is related to the natural log of two divided by the K_a." Tr. 489:25-490:1 (Forrest); Forrest Demonstratives Slide 54; *see also* Tr. 576:3 (Sommi) ("So half-life equals 0.693 divided by K_a.").

171. Based on the K_a Dr. Forrest used for modeling a PP3M injection in the gluteal (0.003904) the half-life of PP3M would be 179 days. Tr. 737:25-738:14, 739:18-22 (Forrest). This is starkly different from the PP3M half-life that he assumed for his 4-5 half-life theory—90 days. FOF 137. Dr. Forrest's theories relied on contradicting scientific assumptions and inaccuracies that were not "close enough" to be used in developing dosing regimens. Tr. 817:24-818:11 (Gobburu).

172. Further highlighting the scientific flaws in Dr. Forrest's approach, plugging the K_a Dr. Forrest used for modeling PP1M in the gluteal (0.0117) into the same equation, the half-life of PP1M would be calculated to be about 60 days, or twice the 30-day half-life Dr. Forrest assumed in his 4-5 half-life theory, and more than the longest known half-life of PP1M, *i.e.*, 49 days. Tr. 576:3-577:3, 577:4-9, 593:13-19 (Sommi).

173. Faced with this damning inconsistency, Dr. Forrest alluded to some distinction between half-life for multi-dose versus single-dose injections. Tr. 738:11-16 (Forrest). But this multi-dose/single-dose distinction has no basis in science; as Dr. Gobburu credibly explained, the "half-life of a drug . . . is constant

over single to repeated dosing in patients. So the half-life would remain the same for paliperidone absorption." Tr. 818:15-819:14 (Gobburu).

174. A POSA would have had no reason to expect Dr. Forrest's methods to accurately predict the pharmacokinetics of PP3M. *See* Tr. 818:7-11 (Gobburu).

d. Dr. Forrest's Alleged "Validation" Required Selective Application and Purposeful Ignorance

175. To validate that their pop-PK model of PP1M, the authors of Samtani 2009 used data from two different clinical studies, "includ[ing] 394 (21.9%) subjects who contributed to 2776 (15%) plasma samples." PTX-118 at 2. That stands in stark contrast to Dr. Forrest's approach to "validating" his PK model.

176. Specifically, to "validate that [his] model that [he] created was working correctly, just at least based on a PP1M formulation," Dr. Forrest used a handful of median plasma concentration data points for ***only one dose*** of PP1M (the 100 mg eq. dose) extracted from Figure 1a of Samtani 2009. Tr. 506:9-22 (Forrest). This was not reasonable. As Dr. Gobburu credibly explained, "there is a discordance between when the actual data . . . rise up to the peak versus when the [projected concentrations] raises up to its peak, and the difference in simple terms between the two is about eight days." Tr. 825:16-826:5 (Gobburu); Gobburu Demonstratives Slide 15. The discrepancy is significant; "[e]ight days of 28 days is more than 25%" and that amount of drug is simply unaccounted for in Dr. Forrest's model. Tr. 826:6-17 (Gobburu). These inaccuracies were not "close enough" to

validate Dr. Forrest's model, much less reliably predict plasma concentrations for use in developing dosing regimens. Tr. 826:6-11, 826:25-827:15 (Gobburu).

177. Dr. Forrest relied on his flawed model to project that plasma concentrations would reach or drop below the minimum of the therapeutic window (or 7.5 ng/mL) at 9 months so that should set the back end of the dosing window at 9 months. Tr. 512:25-513:7 (Forrest); Tr. 584:1-7 (Sommi).

178. But Dr. Forrest picked only the 350 mg eq. dose of PP3M to simulate in his model. Tr. 740:17-25 (Forrest). Dr. Forrest did not attempt to model the three other known doses of PP3M (175, 263 and 525 mg eq.). Tr. 740:13-16 (Forrest). That is not an approach a POSA would take; knowing the available PP3M doses, a POSA would have simulated them all. Tr. 580:23-581:4 (Sommi).

179. But if a POSA were to simulate only one PP3M dose, it would have been the highest 525 mg eq. dose, consistent with the teachings of Samtani 2011.[16]

[16] Samtani 2011 is titled "Dosing and Switching Strategies for Paliperidone Palmitate: Based on Population Pharmacokinetic Modelling and Clinical Data." PTX-161 at 1. Samtani 2011 taught that missed dose regimens are generally designed through studying the PK of a drug, and simulating missed dose scenarios using PK models. PTX-161 at 12 ("approach to the management of missed doses is based on the results of model-based PK simulations"). Samtani 2011 discloses that "[s]imulations also demonstrate that 6 months after stopping paliperidone palmitate therapy, even at the highest dose of 150 mg eq., the median paliperidone plasma concentration would be expected to fall below the level predicted to be required for antipsychotic efficacy (7.5 ng/mL) . . . indicating that re-initiation of treatment should begin *de novo*" before 6 months. PTX-161 at 13. This evidences that the highest dose of PP1M had been used to select the reinitiation regimen for PP1M.

Tr. 581:21-582:12 (Sommi); *see also* PTX-192 at 55 ("These missed dose simulations were performed at the highest PP3M dose strength to assess whether the proposed re-initiation regimen does not produce an overshoot in plasma paliperidone concentrations."). The reason being that, at "the point in time at which there's almost no drug left in the body . . . people with the highest dose are going to have the highest leftover concentrations." Tr. 581:5-581:11 (Sommi). "[I]f you don't get it right . . . and you restart them [*de novo*], they've got too much left, you run the risk of overshooting your target concentration and you get side effects." Tr. 581:12-20 (Sommi). "That's important for long-acting injections because you can't pull them back out." Tr. 581:18-20 (Sommi).

180. If Dr. Forrest had simulated the highest 525 mg eq. dose, he would not have arrived at the 9-month back end because "the highest dose [is] going to have the highest leftover concentrations," so the time to cross the 7.5 ng/mL threshold would have been "at some point in time after the nine months." Tr. 581:9-11, 584:8-15 (Sommi). Conversely, if Dr. Forrest had simulated a dose smaller than 350 mg eq., the time to cross the 7.5 ng/mL threshold would have been sooner than 9 months. Tr. 584:22-24 (Sommi). Dr. Forrest's selection of only the 350 mg eq. dose shows that his PK modeling was engineered to fit the parameters of the Asserted Claims using hindsight—*i.e.*, he did only what would get to the 9-month back end date that he targeted.

B. No Motivation to Combine or Reasonable Expectation of Success

181. Mylan failed to prove its obviousness case. Dr. Forrest was unable to identify key elements of the asserted claims in the prior art. FOF 109. And because the prior art lacks key elements of the Asserted Claims, "a POSA would not be motivated to combine them, and then there would be no reasonable expectation for success in coming to the claim." Tr. 538:21-539:1, 598:16-21 (Sommi). Dr. Forrest's selective and hindsight-driven reliance on certain portions of the PP1M prior art to fill some gaps in the prior art, his ever-shifting and inconsistent uses of these references, and his oversimplified and unscientific modeling, failed to credibly establish obviousness. FOF 119-180.

182. But even if Dr. Forrest's flawed theories were accepted, his testimony would still be insufficient to establish obviousness. Dr. Forrest did not even attempt to articulate a POSA's motivation to arrive at all elements of the Asserted Claims: he did not suggest that the prior art provided motivation to give a patient a dose of PP3M ***before*** they had been clinically stabilized on PP1M for several months, or to sequence different formulations of LAIs in a missed dose regimen such that a patient was given PP1M after being advanced to PP3M. Without directly addressing these deficiencies, and using the Asserted Claims as a roadmap, Dr. Forrest compared the claims to the PP1M prior art and provided an unsubstantiated opinion that the timing and the location of the injections are the same so it would

have all been obvious. Tr. 461:21-462:3 (Forrest). This fails to establish either a motivation to combine or a reasonable expectation of success, which are requirements for establishing obviousness.

1. No Motivation to Treat the 4-9 Month Patient Population with a Reasonable Expectation of Success

183. Dr. Forrest spent the greater part of his trial testimony attempting to establish the 4-9 month intermediate window as obvious, Tr. 588:3-8 (Sommi), but he failed to articulate a motivation to do so, much less a reasonable expectation of success in doing so.

184. Dr. Forrest attempted to identify the 4-month front end of the window using arithmetic multipliers he extrapolated from the Invega Sustenna Label. FOF 119-127. A POSA would have had no reasonable expectation of success in extrapolating in this manner. Tr. 558:15-19 (Sommi). Indeed, Dr. Forrest admitted that this is tantamount to "guessing." Tr. 709:11-14 (Forrest).

185. Dr. Forrest eschewed this approach for the back end as "oversimplifying." Tr. 711:10-14 (Forrest); Tr. 559:14-18 (Sommi). But good science demands that, "if you're going to use this strategy to identify what the window is supposed to be, you should be able to identify the window for the front half and the back half." Tr. 559:19-560:1 (Sommi). Dr. Forrest's failure to do so evidences his use of hindsight and admits that a POSA would not have been motivated to use this approach much less with a reasonable expectation of success.

186. Dr. Forrest's pivot to his 4-5 half-life theory only gets him to a 12-18-month back end; not the 9-month target. Tr. 464:24-465:6 (Forrest). If a POSA were to rely on that theory, they would not have had a reasonable expectation of success in arriving at the 9-month back end.

187. Dr. Forrest's reliance on JAMA to get to the 9-month back end was also flawed. First, JAMA "is not a missed dose study. It's not a drug withdrawal study in the sense of mimicking a missed dose. This is a study to show that the drug works." Tr. 649:18-20 (Sommi). It would ***not*** have been reasonable for a POSA to use any extrapolation theory from JAMA—either from the interim or the final analysis—to try to determine when and how to reinitiate. Tr. 665:15-19 (Sommi).

188. Moreover, Dr. Forrest's reliance on the interim analysis from JAMA, ignoring additional data reflected in the final analysis, FOF 141-143, was scientifically unreasonable. As Dr. Forrest admitted on cross examination, a POSA would "use all the data you had at hand." Tr. 720:1 (Forrest). Dr. Sommi was "astounded" by Dr. Forrest's failure to account for "all the data from a study." Tr. 545:25-546:3; 547:17-19 (Sommi).

189. The final analysis reported that the median time to relapse for placebo patients was 395 days or about 13 months. Tr. 549:9-11 (Sommi). If anything, that

would have led a POSA to a 16-month back end date which "teaches away from nine months." Tr. 548:16-549:22 (Sommi).

190. Even with the interim analysis, a POSA would not have arrived at the 9-month back end with a reasonable expectation of success because the median time to relapse for placebo patients in the interim analysis was 274 days (*i.e.*, about 12 months after the patients' last dose of PP3M). Tr. 547:20-548:9 (Sommi). That too "teaches away from nine months." Tr. 548:16-549:22 (Sommi). And that is consistent with JAMA's teaching that "[p]atients at risk for sudden discontinuation from treatment could therefore benefit from 3-month paliperidone palmitate, providing protection from relapse for ***up to 1 year after the last dose***." PTX-113 at 7. Contrary to Dr. Forrest's "natural jump" opinion, nothing in JAMA suggested 180 days. Tr. 661:5-8 (Sommi) (Dr. Forrest "just picked a day").

2. No Motivation to Use or Reasonable Expectation of Success in Using PP1M After a Patient Had Been Advanced to PP3M

191. Prior to the 693 Patent, there was ***no*** LAIA that recommended using two different long-acting injectable formulations to manage a missed dose. Tr. 557:14-17 (Sommi).

192. The Invega Sustenna Label instructs to "resume the same dose [of Invega Sustenna] the patient was previously stabilized on." Tr. 556:19-557:6, 589:18-21 (Sommi); PTX-106 at 5. For PP1M missed doses, that means reinitiating

with PP1M (not a different formulation), Tr. 704:21-705:5 (Forrest), at the same dose that was missed (except for the highest dose), Tr. 705:9-13 (Forrest). Nothing would have suggested using a formulation other than PP3M to reinitiate a patient that had been advanced to PP3M. Tr. 555:5-7 (Sommi); Tr. 741:7-12 (Forrest) ("the prior art just teaches giving PP1M, then PP3M").

193. A POSA would not have looked to the Invega Sustenna Label to suggest using two different LAIAs to manage a missed dose. Tr. 557:7-13 (Sommi). If anything, a POSA developing a missed dose regimen for PP3M would have given "the dose of PP3M that they missed." Tr. 589:17-590:4 (Sommi).

194. Mylan's own expert Dr. Berger—who, unlike Dr. Forrest, has 50 years of clinical experience with antipsychotics, Tr. 159:14-23 (Berger)—agrees with Dr. Sommi, testifying, repeatedly and without qualification, that "before Invega Trinza came out" (*i.e.*, before the effective filing date of the 693 Patent), treating a patient who had missed a dose of PP3M with PP1M catch-up doses would have been "a bad idea" that was "unsafe," "unreasonable," and "unwise." Tr. 262:9-263:9, 1048:9-22 (Berger). Although Mylan's counsel subsequently solicited Dr. Berger to retract this position, he declined to do so, instead reiterating his view that it was "far safer" and "far wiser" to reinitiate nonadherent patients directly on PP3M rather than by using the dosing regimen of the Asserted Claims. Tr. 1043:5-24 (Berger). Contrary to Dr. Forrest, Dr. Berger—even with the benefit of Invega

Trinza's missed dose instruction—sees no reason to use PP1M after a patient has been advanced to PP3M, and has no reasonable expectation of success in doing so.

195. Dr. Forrest's supposed rationale for using PP1M after a patient advanced to PP3M is that, in his opinion, a POSA would have known that PP1M is "faster acting" and "it was known that a PP1M could be used to load them up with drug pretty rapidly so they would be in steady state range for their repeat injections." Tr. 413:20-414:3; Tr. 741:13-18 (Forrest).

196. Dr. Forrest was unable to point to any credible evidence that would have taught that PP1M reaches therapeutic levels any faster than PP3M. Tr. 742:5-11 (Forrest).[17] Dr. Forrest seemed to suggest PP1M is faster acting because PP3M may include larger particle sizes that are slower to absorb.[18] Tr. 400:25-401:5, 406:19-407:3, 410:9-12 (Forrest). But the fact that PP3M may include larger

[17] Dr. Forrest opined that the minimum therapeutic plasma concentration for paliperidone is 7.5 ng/mL. Tr. 584:1-5 (Sommi); Tr. 422:6-8 (Forrest). Dr. Forrest readily admitted on redirect, in attempting to rehabilitate his opinions based on his modeling, that PP3M "reaches 7.5 [ng/mL] more quickly because there is 3.5 times as much dosage in addition" as compared to PP1M. Tr. 784:20-23 (Forrest).

[18] Dr. Forrest relied on a theory "from over 40 years ago" about a vague relationship that as particle size increases absorption rate slows as purported rationale for using PP1M after patient had been advanced to PP3M. Tr. 409:22-410:12 (Forrest). Dr. Forrest also relied on a sugar analogy to make a similar point, Tr. 407:15-408:6 (Forrest), but he later disavowed this analogy "because sugar is pretty soluble," Tr. 787:22-24 (Forrest). Whichever theory or analogy Dr. Forrest used, because the art lacked PK data about PP3M, a POSA would have had no reason to believe that PP1M would reach therapeutic concentrations faster than PP3M when used for reinitiation. Tr. 594:16-595:7 (Sommi).

particles than PP1M "would account for the back end of why you can dose this drug for three months," it does not predict anything about what happens at the initial burst. Tr. 594:16-595:7 (Sommi) ("We don't know anything about the initial release.").

197. As both Drs. Gobburu and Sommi explained, since the art lacked PK data about PP3M, a POSA would have had no reason to believe that PP1M would reach therapeutic concentrations faster than PP3M when used for reinitiation. Tr. 593:24-594:13 (Sommi); Tr. 827:24-828:10 (Gobburu); Shaw Dep. Tr. 136:9-12.

198. Nothing in the prior art would have motivated a POSA to use PP1M after a patient advanced to PP3M. Tr. 598:11-13, 598:16-17 (Sommi). Nor would there have been any reasonable expectation that PP1M would reach therapeutic levels more rapidly than PP3M. Tr. 593:24-594:9, 598:18-21 (Sommi).

199. Indeed, if a POSA were to rely on Dr. Forrest's flawed modeling—which a POSA would not have done—it would suggest that PP1M is absorbed no faster than PP3M. Tr. 828:15-25 (Gobburu). A POSA would have understood Dr. Forrest's graph to show that the initial rise of concentration of "PP1M is about the same as PP3M." Tr. 592:14-17 (Sommi); Tr. 828:22-23 (Gobburu) ("Both PP1M and PP3M are superimposed, identical pretty much."); Gobburu Demonstratives

Slide 18; PTX-100D at 2 (compare blue line and green line at times 0-10 days).[19] "There is no reason for Forrest to reinitiate the patient who missed [PP]3M dosing with PP1M, the monthly injection." Tr. 813:17-22 (Gobburu).

200. Dr. Forrest admitted on cross-examination that, according to his own simulated predictions, there was no difference in speed between the initial absorption of PP1M and PP3M. Tr. 745:8-746:3, 746:18-25 (Forrest); PTX-100D at 2; Gobburu Demonstratives Slide 18. And this was true even though his comparison was skewed to favor faster absorption of PP1M; as Dr. Forrest admitted, he compared the projected concentrations following 100 mg eq. of PP1M in the ***deltoid*** versus 350 mg eq. of PP3M in the ***gluteal***. Tr. 748:6-10 (Forrest); Tr. 596:2-9 (Sommi). But deltoid injections result in faster rise in initial plasma concentration than gluteal injections, facilitating a more rapid attainment of therapeutic concentrations. Tr. 726:25-727:2, 747:15-20 (Forrest); Tr. 596:2-4 (Sommi); Tr. 829:6-8 (Gobburu).

201. Dr. Forrest "could have modeled PP1M deltoid to PP3M deltoid," but he inexplicably chose not to do so. Tr. 596:2-9 (Sommi). Perhaps because, if he had, as Dr. Forrest admitted, the initial concentration rise for ***PP3M*** "would have

[19] Dr. Forrest testified that putting these figures on the same graph was not to compare the data, but "to save space and condense. Best intentions." Tr. 784:9-785:9 (Forrest); Tr. 747:23-748:10 (Forrest) ("[T]hey're not comparing those two. This was just validation. I put them on the same chart for space considerations."). That *post hoc* rationale lacks credibility on its face.

been faster." Tr. 749:10-14 (Forrest); Tr. 829:13-17 (Gobburu) ("Then PP3M would be faster than PP1M."). This would have completely undermined Dr. Forrest's assumption that PP1M is a "faster acting" version. Tr. 741:13-18 (Forrest).

202. In short, a POSA relying on Dr. Forrest's modeling-based approach would have had no reason or motivation to reinitiate PP3M patients in an intermediate time window using PP1M, and, if anything, would have been led away from using PP1M. *See* Tr. 829:13-22 (Gobburu).

203. If a POSA had believed (without data one way or the other) that PP3M would release drug too slowly to be used for reinitiation, then a POSA would have used oral supplementation. Tr. 749:15-19 (Forrest); Tr. 591:19-592:4 (Sommi) (oral is "the most quickly absorbed of any formulation" so "if you want to get those concentrations back up very, very quickly, oral is the way to go").

204. This approach is consistent with teachings in the prior art. For example, patients missing an injection of Abilify Maintena received an injection of Abilify Maintena supplemented with oral Abilify. Tr. 590:21-591:9 (Sommi); PTX-168 at 3-4. The Risperdal Consta label also instructed to give the missed Risperdal Consta injection and supplement with oral antipsychotic, and taught using this approach when "there are no data to specifically address reinitiation of treatment." Tr. 591:10-18 (Sommi); PTX-187 at 7. Without actual data on the PK

of PP3M in hand, a POSA would, if anything, have been motivated to give the missed dose of PP3M and supplement with oral paliperidone.

3. No Motivation to Use PP3M Without Stabilizing with Four or More Months of PP1M with a Reasonable Expectation of Success

205. There was also no motivation to use PP3M without first stabilizing the patient for four or more months on PP1M. All of the PP3M references relied on by Dr. Forrest required patients to be stabilized on PP1M for at least 4 months before advancing to PP3M. In the placebo-controlled study—as described in JAMA and the 2014 Press Release—all patients were stabilized on PP1M for ***17 weeks*** before advancing to PP3M. Tr. 542:3-9, 553:10-15, 645:18-21 (Sommi). Similarly, in the study that compared PP3M to PP1M—as described in NCT 423—"[e]verybody was given PP1M" for ***17 weeks*** to be stabilized on PP1M before half the patients advanced to PP3M. Tr. 541:11-18 (Sommi).

206. Thus, if a patient who missed a dose of PP3M were given PP1M, there would have been no reason or motivation to advance them to PP3M without first stabilizing them on PP1M for at least 17 weeks, since that was the only way PP3M was reportedly used in the prior art. *See* Tr. 686:2-14 (Forrest).

C. Dr. Forrest's Opinions are Not Credible Evidence of Obviousness

207. Although he had no experience with antipsychotics, treating psychotic disorders, direct patient care, or paliperidone prior to this case, Dr. Forrest has

substantial experience serving as an expert witness for generic pharmaceutical companies such as Mylan. Tr. 523:14-19 (Forrest). Among the 16 cases in which he has testified for patent challengers, when there was a validity issue, he has ***never*** testified that a patent is valid. Tr. 523:14-19, 770:16-18 (Forrest).

208. Dr. Forrest's testimony was not credible, falling far short of providing clear and convincing evidence of obviousness. His opinions are infected with hindsight, as evidenced, for example, through his admission that Mylan's counsel provided copies of the references and the specific combinations that he relied on to support obviousness. Tr. 678:14-25 (Forrest). Dr. Forrest simply agreed with them, thus allowing his 189-page expert report to be completed within a matter of weeks, while at the same time he was preparing an expert report on invalidity of two other patents and maintaining a full-time job as a professor. Tr. 679:1-680:2 (Forrest).

209. Dr. Forrest repeatedly shifted his theories to arrive at the target he could only have known using hindsight based on the claims, not based on any cogent scientific rationale. FOF 119-151. "It was clear that [Dr. Forrest] kept adjusting to get to where he needed to be in four to nine months." Tr. 597:20-598:2 (Sommi).

210. Dr. Forrest's obfuscating and evasive testimony defending his ever-shifting theories severely undermined his credibility.[20] For example, Dr. Forrest revealed at trial a never-before-disclosed "natural jump" theory based on JAMA to arrive at the 9-month back end of the intermediate window. FOF 150. When asked (repeatedly) whether the 180-day theory appeared in his expert report or deposition or anywhere else prior to trial, Dr. Forrest refused to give a straight answer.[21] Tr. 698:9-22, 700:14-22, 701:15-20 (Forrest). Because the truth is, Dr. Forrest "didn't say anything about 180 days" before trial. Tr. 660:25-661:4, 665:24-666:4 (Sommi). Dr. Forrest's repeated refusal to answer direct questions on at trial is tantamount to an admission that he had in fact changed his theory after being proved wrong at deposition. *See* Tr. 698:24-699:24 (Forrest).

211. Further revealing the lack of credible testimony, Dr. Forrest disputed facts that could not be plausibly denied. For example, Dr. Forrest presented text from the 536 Publication without the accompanying table, FOF 135-136, testifying that the 536 Publication was "all about paliperidone palmitate," Tr. 430:4-6, 714:10-715:10 (Forrest), when the very table on which he relied did not include

[20] Dr. Forrest's impeachments were not isolated incidents. Throughout cross-examination, Dr. Forrest repeatedly contradicted his deposition testimony and expert reports. *See, e.g.*, Tr. 709:20-710:10; Tr. 721:20-722:6; Tr. 726:1-10 (Forrest).

[21] In contrast, the testimonies of Drs. Sommi and Gobburu on non-obviousness were credible as demonstrated by their direct, honest, fair and objective answers provided throughout cross-examination.

paliperidone palmitate, Tr. 562:10-11 (Sommi); PTX-116 at 19. When confronted with this on cross examination, Dr. Forrest quarreled rather than confess his misdirection. Tr. 715:18-716:12 (Forrest).

212. Dr. Forrest was also caught obfuscating facts during a probe of his modeling. Dr. Forrest simulated only one dose (100 mg eq. dose of PP1M in the deltoid). Tr. 731:21-732:4, 732:14-18 (Forrest); PTX-100D at 2. He failed to simulate the 25, 50 or 150 mg eq. doses of PP1M, Tr. 732:19-22, 733:9-13 (Forrest), even though "there was nothing that would have prevented him from doing that," Tr. 579:6-20 (Sommi). On cross-examination, Dr. Forrest attempted to defend his cherry-picking of a single dose by asserting that it would have been "duplicative" because the four doses "had linear PK." Tr. 733:11-14, 733:21-25 (Forrest). That was untrue; only after Janssen's counsel pointed out on cross examination that the C_{max} of the four PP1M doses in Figure 1A are ***not*** linear did Dr. Forrest reluctantly admit that "C_{max} was not quite linear" and "was not quite dose proportional." Tr. 734:1-4 (Forrest); *accord* Tr. 824:8-19 (Gobburu).

213. The presentation of Dr. Forrest's modeling output was also misleading. Dr. Forrest's supposed rationale for reinitiating with PP1M is that PP1M is a "faster acting" version. Tr. 741:13-18 (Forrest). However, Dr. Forrest's own PK modeling figure (PTX-100D at 2) provides a side-by-side comparison of ***PP1M*** injected in the ***deltoid*** and ***PP3M*** injected in the ***gluteal***, when Dr. Forrest

knew that PP3M injected in the deltoid would have been absorbed even faster. FOF 200-201. Recognizing that the figure he presented to the Court as the output of his modeling was not an apples-to-apples comparison but was skewed in favor of the point he was trying to make, Dr. Forrest offered the ludicrous excuse that he was "not comparing those two" he simply "put them on the same chart for space considerations." Tr. 747:21-748:10 (Forrest). Trying to defend this indefensible position on redirect, Tr. 784:9-785:9 (Forrest), Dr. Forrest admitted that a POSA would, in fact, have expected PP3M to reach therapeutic levels faster than PP1M. Tr. 784:20-23 (Forrest).

D. Objective Indicia Provide Real-World Evidence of the Nonobviousness of the Claims

214. It is undisputed that dosing Invega Trinza according to its label for patients who last received a dose of PP3M between 4 and 9 months ago practices the Asserted Claims. Tr. 93:2-5 (Sommi); Tr. 244:12-14, 1038:2-10 (Berger). The real-world evidence concerning Invega Trinza therefore constitutes objective evidence corroborating that the Asserted Claims would not have been obvious.

1. Long-Felt Need

a. Invega Trinza Met a Long-Felt Need For a Three-Month LAI Anti-Psychotic

215. Patient non-adherence is a persistent challenge in treating schizophrenia. Tr. 871:24-873:6 (Kohler); 1060:17-25 (Berger). LAIAs were developed to address this challenge by reducing the number and frequency of doses

patients must take. Tr. 873:13-23 (Kohler); 1034:24-1035:6 (Berger). Longer dosing intervals provide a promising pathway to better adherence for patients who struggle to maintain a daily oral medication regimen. Tr. 873:13-23 (Kohler).

216. Although because HCPs administer LAIAs, this facilitates better adherence monitoring, LAIAs also have disadvantages. First, longer dosing intervals elevate the risk of sustained and debilitating side effects. Tr. 875:9-18 (Kohler). These can include painful muscle contractions in the neck and throat or extreme restlessness. Tr. 872:14-24 (Kohler). Unlike oral medications, which are metabolized in a matter of days, LAIAs remain in the body for weeks or months. Tr. 875:9-18 (Kohler). As a result, side effects may linger for much longer and require additional medication or even hospitalization. Tr. 875:19-24 (Kohler).

217. Second, patients must present to an HCP to receive their medication when being treated with LAIAs. Tr. 874:15-18 (Kohler). Returning for medication frequently can be challenging for patients who must balance their treatment of schizophrenia with their other life responsibilities. Tr. 874:16-21 (Kohler). As of 2015, there were four second-generation LAIAs on the market in the U.S., with dosing intervals ranging from two weeks to five weeks. Tr. 874:3-10 (Kohler); PTX-089C at 10. Given these relatively short dosing intervals, there "definitely was a need" for an LAIA with a longer dosing interval in 2015. Tr. 874:13-15 (Kohler).

218. Invega Trinza met the need for longer-acting antipsychotic—offering a three-month dosing interval that was more than twice as long as any LAIA on the market at the time. Tr. 876:5-9 (Kohler). Dr. Kohler testified that Trinza was ultimately "very well received" by the field and that the medication "frees" patients to pursue a "more independent functioning" lifestyle. Tr. 876:4, 883:24-884:3 (Kohler). Dr. Berger agreed it is "a wonderful drug." Tr. 1058:21-24 (Berger).

b. The Missed-Dose Instructions of the Asserted Claims Contributed to Invega Trinza's Fulfillment of the Long-Felt Need

219. Invega Trinza did not eliminate the issue of nonadherence. Tr. 884:4-7 (Kohler); 1060:17-19 (Berger). Given that the patients treated with LAIAs have already demonstrated difficulty adhering to medication, Dr. Kohler explained that it is likely that "nonadherence will occur again." Tr. 884:4-7 (Kohler).

220. Nonadherence to a LAIA with a 3-month dosing interval presents special challenges. Undertreatment could lead to relapse. Tr. 886:4-5 (Kohler). Overtreatment could lead to debilitating side effects that prevent continuing with a medication. Tr. 886:8-10 (Kohler). This delicate balance between relapse and side effects is further complicated by clinicians' "limited knowledge about pharmacokinetics, pharmacodynamics [and] how long the product lasts to exert clinical efficacy." Tr. 889:15-17 (Kohler). As a result, clinicians "have to have clear instructions about how to catch a person up to the previously effective

treatment regimen"; they should not "experiment" on their patients with limited pharmacological knowledge. Tr. 884:8-10, 886:4 (Kohler). Thus, without the patented missed dose instructions, clinicians "would have been very reluctant in transferring stable patients on Invega Sustenna to Invega Trinza," Tr. 889:21-24 (Kohler), and Invega Trinza would not have met the long-felt need for a longer-acting LAI.

2. Commercial Success

a. Invega Trinza Is a Marketplace Success

221. Consistent with Dr. Kohler and Dr. Berger's praise for the product, "Invega Trinza's been a success in the marketplace" by multiple economic metrics. Tr. 1088:17-18 (Mulhern)

222. **Sales.** Invega Trinza has generated more than $2.5 billion in sales since launch. Tr. 1083:16 (Mulhern); Tr. 1160:10-13 (Stec); PTX-089C at 3; PTX-530. Sales have grown substantially, with an annual compound growth rate of 22.2% since launch, and net sales of $570 million in 2021. Tr. 1083:13-18 (Mulhern); Mulhern Demonstratives Slide 4; PTX-089C at 3; PTX-530. Mylan does not dispute this. Tr. 1160:6-9 (Stec).

223. **Market Share.** The market for LAIAs is crowded and competitive. Tr. 1084:19-21 (Mulhern). With nine second-generation LAIAs introduced since the early 2000s, both the "sheer number" of competitor products and the timeline of

product launches provide evidence "that this is a very competitive marketplace." Tr. 1084:19-21.

224. In this crowded market, Invega Trinza has captured the third-highest share of both days of treatment and sales among second-generation LAIAs, representing 8.8% of the total days of treatment and 12.6% of the revenue generated by LAIAs in 2021. Tr. 1086:1-3; 1086:21-24 (Mulhern); PTX-089C; PTX-410; PTX-528. [redacted] PTX-089C at 48; PTX-410.

225. Among paliperidone palmitate LAIAs, Invega Trinza accounted for 28.1% of the days of treatment for patients eligible to switch from Invega Sustenna in 2021, which is particularly notable because such patients are, by definition, adequately treated by Invega Sustenna and not required to switch to Invega Trinza. Tr. 1088:1-12 (Mulhern); Mulhern Demonstratives Slide 8; PTX-089C at 25-27, 29-30.

b. There is a Nexus Between the Asserted Claims and Invega Trinza's Marketplace Success

226. There is a nexus between the Asserted Claims and Invega Trinza's commercial success because the missed dose instructions set forth in the Asserted Claims contribute to a HCP's decision to prescribe Invega Trinza. Tr. 889:21-24, 892:11-16 (Kohler); 1096:17-20, 1100:2-8, 1101:5-7 (Mulhern). Although the missed dose instructions are not the sole driver of Invega Trinza's commercial

success, the Asserted Claims "enable[] the safe and effective treatment in the event of a missed dose of Invega Trinza." Tr. 1091:20-21 (Mulhern), which is "very important" when considering whether to prescribe Invega Trinza. Tr. 889:17-18 (Kohler). As Ms. Mulhern explained, there usually are multiple factors with a nexus to the commercial success of a product. Tr. 1089:2-5 (Mulhern). For example, Ms. Mulhern noted that the slide-to-unlock feature of the iPhone has a nexus to the iPhone's commercial success, even though "there are lots of factors that drive a purchase decision for the iPhone." Tr. 1089:5-8 (Mulhern).

227. Given the strong potential for missed doses, clear instructions for resuming treatment following a missed dose are important to the safety and long-term efficacy of a LAIA. Tr. 884:8-13 (Kohler). Without such instructions, a clinician would be left to "experiment" on patients with limited knowledge of the practical aspects of re-initiation, including the pharmacokinetic profile of the drug necessary to determine the appropriate dose, timing, and product to be used to resume treatment. Tr. 886:2-10; 890:10-22, 891:23-892:3 (Kohler); PTX-97 at 17. For precisely this reason, a peer reviewed paper found that the lack of clear directions for re-initiating after a missed dose contributes to clinicians' reluctance to prescribe certain LAIAs in the first instance. PTX-97 at 17.

228. The role of missed dose instructions in driving the decision to prescribe Invega Trinza is reinforced by Janssen's own marketing materials. Tr.

1092:6-9; 1094:9-1096:12 (Mulhern); PTX-449 at 1; PTX-509 at 62, 64, 66-68, 76; PTX-510 at 45, 47, 49-51, 58; PTX-513 at 75. Not only does Janssen present the missed dose instructions prominently in its marketing materials and sales training documents, it has even created a specific website to educate clinicians about the pharmacokinetics of Invega Trinza's dosing instructions—including the patented missed dose instructions. Tr. 1095:12-1096:3 (Mulhern); PTX-449.

229. Invega Trinza's relationship with Invega Sustenna provides further evidence of the role of missed dose instructions in enabling Invega Trinza's success in the marketplace. Tr. 1099:20-1100:8 (Mulhern). It is undisputed that patients must be adequately treated with Invega Sustenna for four months before beginning treatment with Invega Trinza. Tr. 1176:14-18 (Stec). It is also undisputed that switching to Invega Trinza is not required, nor are there any economic pressures to make the switch. Tr. 1176:19-1177:14 (Stec). And it is undisputed that a significant number of patients miss doses of LAIAs. Tr. 884:4-7 (Kohler); 1060:17-19 (Berger). Thus, as Dr. Kohler testified, providers would be very unlikely to switch patients already being adequately treated with one paliperidone palmitate product (Invega Sustenna) to another medication using the same active ingredient (Invega Trinza), unless that second product included clear instructions for how to proceed in the event of a missed dose. Tr. 892:11-23 (Kohler). For this reason, the Asserted Claims "contribute[] to the commercial and clinical

acceptability of switching a stable Invega Sustenna patient to Invega Trinza," Tr. 1091:18-24 (Mulhern), and therefore "contribute to the marketplace success of Invega Trinza," Tr. 1096:17-20 (Mulhern).

230. The patient population addressed by the Asserted Claims is economically significant. Tr. 1161:1-10 (Stec). Dr. Berger testified that more than 50% of his patients on Invega Trinza miss a regularly schedule dose, and of those, 20 to 30% return more than four months after their prior dose. Tr. 251:5-14 (Berger). Dr. Kohler testified that 5 of the 70 patients he has treated with Invega Trinza, or 7%, have missed a dose and returned in the four-to-nine-month window to resume treatment with Invega Trinza according to the Asserted Claims. Tr. 888:17-21 (Kohler). Both experts' experiences are consistent with the literature on the frequency of missed doses. Tr. 1092:24-1094:8 (Mulhern); PTX-220 at 8.

231. Moreover, the nexus between Invega Trinza's commercial success and the Asserted Claims is not limited to sales of doses administered pursuant to the claimed missed dose regimen. As Ms. Mulhern explained, actual use does not capture the full—or even primary—value of a safety feature like the missed dose regimen. Tr. 1100:12-1101:2 (Mulhern). The more important value added by the patented re-initiation regimen is the significant "option value," similar to an airbag or other safety features in a vehicle. *Id.* Ms. Mulhern's testimony was consistent with the testimony of Dr. Kohler, and the literature on which he relied, which

indicated that missed doses instructions influence the decision on whether to switch patients to Invega Trinza in the first place, before the patient has ever missed a dose. FOF 220. For this reason, the Asserted Claims have contributed to the overall success of Invega Trinza. Tr. 1101:5-7 (Mulhern).

c. Mylan Failed to Undermine Janssen's Evidence of Commercial Success

232. Mylan's economic expert, Dr. Stec, did not undermine Janssen's evidence of the commercial success of the Asserted Claims.

233. On the issue of Invega Trinza's marketplace success, Dr. Stec's critique of Ms. Mulhern lacks both credibility and evidentiary support. He asserted that Invega Trinza's $2.5 billion in sales were not necessarily indicative of commercial success, but could not cite any evidence explaining how Invega Trinza's sales were outweighed by costs. Tr. 1160:21-25 (Stec). [redacted] ignoring that this very comparison was the foundation for Ms. Mulhern's conclusion that Invega Trinza is a commercial success. Tr. 1083:23-1087:16 (Mulhern). [redacted]

[redacted]

234. Dr. Stec's position on nexus also lacks support and credibility. He initially testified that he did not agree with Ms. Mulhern that nexus could be established "even if the patented invention is not solely responsible for the commercial success of the product." Tr. 1136:4-10 (Stec). Yet, following impeachment with his contrary deposition testimony, Dr. Stec conceded that the patented invention "does not have to be the sole driver" to establish a nexus to commercial success. 1167:18-19 (Stec). But Dr. Stec still maintained that the patented invention had to be a "primary driver" of commercial success to establish a nexus, Tr. 1167:23-1168:3 (Stec), until later conceding that this, too, was not necessarily true:

> **Q:** If a patented invention contributes but isn't necessarily the primary driver, is it still relevant?
>
> **A:** It potentially could be, but you do an analysis to determine that.

Tr. 1168:16-19 (Stec).

235. Dr. Stec's critiques of Ms. Mulhern's nexus analysis ignored the substance of her trial testimony. For example, he testified that "Ms. Mulhern confuses the three-month dosing interval with the patented regimen or the claims of the patent," Tr. 1127:3-5 (Stec), despite the fact that Ms. Mulhern's nexus analysis

was focused on the specific benefits of the missed dose regimen, as illustrated by her analogy to airbags and her emphasis on the option value of the patented missed dose instructions, Tr. 1100:12-1101:7 (Mulhern). He then suggested that Ms. Mulhern attributed "all the market performance, frankly, of Trinza to the claimed benefits," Tr. 1136:12-14 (Stec), despite Ms. Mulhern's testimony that there are "almost always" multiple drivers of commercial success. Tr. 1089:2-5 (Mulhern).

236. Dr. Stec also offered an unsupported interpretation of the Joshi paper (PTX-220) relied upon by Ms. Mulhern. Specifically, he testified that the patients studied in Joshi "***all*** received the PP3M dose when they came back for that second dose," and therefore "the health care providers in this particular study don't appear to be following the claims . . . of the patent-in-suit." Tr. 1156:13-21, 1180:9-18 (Stec). On cross-examination, however, Dr. Stec admitted that the table he relied on did not actually indicate whether or not patients had received the PP1M re-initiation doses of the Asserted Claims. Tr. 1181:15-1182:7 (Stec). He allowed that, despite his prior testimony that 0% of patients had followed the prescribing guidelines with respect to missed doses, Tr. 1180:17-18 (Stec), it was in fact "possible" that some of them did, Tr. 1182:16-1183:5 (Stec). Dr. Stec also acknowledged that the Joshi study "found that PP3M was generally administered to schizophrenia patients following the prescribing guidelines." Tr. 1183:14-16 (Stec). Dr. Stec's testimony that the Joshi paper showed 0% usage of the Asserted

Claims was not credible, and was ultimately abandoned by Dr. Stec.

237. Dr. Stec conceded that he was not qualified to opine on the clinical factors that cause clinicians to switch a patient to Invega Trinza. Tr. 1177:16-23 (Stec). Although Dr. Stec discounted the opinion of Dr. Kohler that the patented benefits contributed to clinicians' decision to prescribe Invega Trinza, neither Dr. Stec nor Dr. Berger testified that Dr. Kohler was wrong when he testified that Invega Trinza's missed dose instructions play a role in clinicians' prescribing decisions. Tr. 1063:5-8 (Berger); 1178:25-1179:4 (Stec).

238. Furthermore, Dr. Berger agreed with Dr. Kohler that nonadherence was a common occurrence, that treating patients who missed a dose was an important or significant challenge, and that the patented missed dose instructions are "helpful" to clinicians. Tr. 1060:17-1061:5 (Berger). And Dr. Berger did not contend that the basis for his opinion was more reliable than Dr. Kohler's or that Dr. Kohler testified in some way inconsistent with his own clinical experience. Tr. 1062:9-14, 1063:5-8 (Berger). In short, Dr. Berger's testimony does not undermine Dr. Kohler's testimony and experience that the patented missed dose instructions contribute to his and other clinicians' decision to prescribe Invega Trinza.

3. Skepticism

239. Clinicians, including Dr. Berger, have expressed skepticism that the patented missed dose regimen would successfully re-initiate patients on Invega

Trinza. Initially, in service of his non-infringement testimony, Dr. Berger testified that it was "unsafe" and "unreasonable" and a "bad idea" to follow the FDA-approved missed dose regimen set forth in the Asserted Claims. Tr. 262:9-263:9 (Berger). Apparently recognizing that this testimony was harmful to Mylan's case, Dr. Berger, at the prompting of counsel, attempted to walk it back the following week during his testimony on objective indicia, testifying that the Asserted Claims were not unsafe "in all instances." Tr. 1043:5-10 (Berger). But Dr. Berger then went on to reconfirm that it is "far safer" or "far wiser" to ignore the FDA-approved label for Invega Trinza and instead administer the next dose of PP3M to nonadherent patients who return within 4 to 9 months. Tr. 1043:11-24 (Berger). Even in his effort at damage control, Dr. Berger remained skeptical of the dosing regimen of the Asserted Claims.

240. Dr. Berger also recalled that he and his colleagues had questions about whether Invega Trinza would actually provide therapeutic benefit for the full three months of the dosing interval. Tr. 1058:15-19 (Berger). Dr. Kohler likewise testified that clinicians were initially skeptical of Invega Trinza's long dosing interval, and that the unique re-initiation regimen set out in the Asserted Claims could create a "particular challenge," due to its requirement that patients return to their HCP three times in 35 days. Tr. 885:14-18, 889:13-18 (Kohler).

VII. MYLAN FAILED TO ESTABLISH THAT THE ASSERTED CLAIMS ARE INVALID UNDER 35 USC § 112

241. Dr. Forrest opined that the terms PP1M and PP3M as used in the Asserted Claims are not enabled and lack written description under 35 U.S.C. § 112 ("Section 112"), but his conclusory opinions were unpersuasive. Tr. 516:1-523:9, 754:6-10 (Forrest). These opinions were offered only in the alternative, ignore the substantial disclosure about PP1M and PP3M in the 693 Patent, and repeatedly fail to incorporate the knowledge and perspective of a POSA.

A. Mylan's Expert Did Not Endorse Mylan's Section 112 Invalidity Theory

242. Mylan's sole 112 expert, Dr. Forrest, did not endorse Mylan's 112 invalidity theories. Dr. Forrest provided cursory enablement and written description opinions, but made clear that his opinions were exclusively in the alternative to his obviousness opinion: "***[i]f the claims aren't obvious***, then [they] are invalid because they lack enablement" and "[t]hose same claims are, ***if not obvious***, invalid because they lack sufficient written description." Tr. 516:1-8 (Forrest); *see also* Tr. 750:17-751:2 (Forrest).

243. Dr. Forrest does not agree with his own testimony that the Asserted Claims are invalid under Section 112. For example, Dr. Forrest acknowledged that in forming his enablement opinion, he made an assumption that the art was unpredictable, but confessed that he did not actually believe that:

> **Q.** For purposes of your enablement opinion, you assumed that the use of a multi-dose paliperidone palmitate dosing regimen was unpredictable, right?
>
> **A.** In the context of enablement, yes.
>
> **Q.** But you don't actually believe that? You do not actually believe that?
>
> **A.** As I stated for obviousness, no. I think it is predictable, but for purposes of enablement analysis, I have to use a different standard.

Tr. 752:2-10 (Forrest).

244. Dr. Forrest was forced to admit that he did not have an abiding conviction that the claims are invalid under Section 112. When asked at deposition "if it was [his] abiding or strong conviction that the claims are obvious or [his] strong conviction that the claims are invalid under 112," Dr. Forrest could only respond "that the claims are obvious, and ***if not obvious***, then the claims are invalid for some other reason." Tr. 769:21-770:2 (Forrest); *see also* Tr. 750:17-751:2 (Forrest). Dr. Forrest's testimony therefore fails, on its face, to establish by clear and convincing evidence that the Asserted Claims are invalid under Section 112.

B. Mylan Failed to Establish that the Asserted Claims are Non-Enabled

245. Setting aside Dr. Forrest's lack of belief in Mylan's Section 112 theories, his testimony failed to establish that the Asserted Claims are not enabled. Dr. Forrest does dispute that the claimed dosing regimens are enabled. Tr. 516:24-517:22 (Forrest);Tr. 956:12-17 (Little). Rather, the crux of Mylan's non-

enablement opinion is that a POSA could not practice the full scope of the Asserted Claims without "a lot" of experimentation because (1) the Asserted Claims do not specify the particle size or preferred excipients and concentrations for PP1M and PP3M and the terms are therefore very broad, and (2) there are "no working examples" in the 693 Patent. Tr. 516:21-517:11, 518:3-519:2, 754:6-10 (Forrest). Mylan is incorrect on both counts.

1. The 693 Patent Specification Provides Ample Information to Practice the Full Scope of the Asserted Claims

246. Although the Asserted Claims do not specify the particle size or excipients (and their concentrations) of PP1M and PP3M, there is no dispute that the ***specification*** of the 693 Patent discloses those features and others. Tr. 962:13-963:7 (Little); Tr. 517:23-518:8 (Forrest). Indeed, the 693 Patent contains "ample information in the specification about all the structural features" of PP1M and PP3M such that the specification "hand[s] a person of ordinary skill in the art the recipes to make PP3M and PP1M" for use in the Asserted Claims. Tr. 962:21-963:4 (Little). Those "recipes" contain "sufficient information for a POSA to be able to make and use the claimed invention." Tr. 963:5-7 (Little).

a. Concentration and Ingredients

247. For starters, the 693 Patent contains a disclosure akin to a recipe for PP1M:

> In particular, such a composition for the 1-month formulation will comprise by weight based on the total volume of the composition: (a) from about 3% to 20% (w/v) of the prodrug; (b) from about 0.5% to 2% (w/v) of a wetting agent; (c) one or more buffering agents sufficient to render the composition neutral to very slightly basic (pH 8.5); (d) from about 0.5% to about 2% (w/v) of a suspending agent; (e) up to about 2% (w/v) preservatives: and (f) water q.s. ad 100%.

PTX-1 at 13:62-14:3; Tr. 964:14-965:8 (Little).

248. The 693 Patent includes a similar recipe-like disclosure for PP3M:

> In particular for the 3-month formulation the composition will be (a) from about 280 to about 350 mg/mL of prodrug; (b) from about 8 to about 12 mg/mL of wetting agent; (c) from about 16 to about 22 mg/mL of one or more buffering agents to render the neutral to very slightly basic (pH 8.5); (d) from about 65 to about 85 mg/mL of a suspending agent; (e) up to about 2% (w/v) preservatives; and (f) water q.s. ad 100%.

PTX-1 at 13:49-56; Tr. 968:24-969:4 (Little).

249. The prodrug referred to in the specification is paliperidone palmitate, and a POSA would be familiar with the classes of listed excipients, including wetting agents, suspending agents, and buffers. Tr. 965:12-23 (Little). The 693 Patent specification includes both lists of exemplary excipients and of preferred excipients for PP1M and PP3M. Tr. 965:14-966:20, 967:7-13 (Little); *see, e.g.*, PTX-1 at 10:1-30, 13:3-13; 4:33-39; 13:56-61; 14:9-13.

b. Particle Size

250. The 693 Patent specification also provides the particle size range for PP3M and PP1M, including preferred particle size ranges:

> The 3-month formulations would have an average[] size of less than about 20 µm to about 3 µm. Preferably the particles would have an average particle size (d50) of from about 10 µm to about 3 µm; preferably about 9 µm to about 4 µm.
>
> The 1-month aqueous formulation would preferably be a nano particle suspension of wherein the nano particles would be of an average[] size of less than about 2,000 nm to about 100 nm. Preferably the nano particles would have an average particle size (d50) of from about 1,600 nm to about 400 nm and most preferably about 1,400 nm to about 900 nm.

PTX-1 at 9:38-01; Tr. 971:5-22 (Little).

c. Manufacturing Information

251. The 693 Patent specification also provides manufacturing instructions:

> The particles of this invention can be prepared by a method comprising the steps of dispersing paliperidone palmitate in a liquid dispersion medium and applying mechanical means in the presence of grinding media to reduce the particle size of the antipsychotic agent to an effective average particle size.

PTX-1 at 11:14-19; Tr. 978:24-979:6 (Little).

252. Dr. Little confirmed that a POSA would know how to prepare the particles as described as it was "commonly known in the field." Tr. 979:7-9 (Little). But, the specification also includes "general types of manufacturing . . . and then specific types of manufacturing" information. Tr. 978:13-23 (Little). For instance, it provides the procedure for grinding the formulation to the desired particle size:

> A general procedure for preparing the particles for the 1-month formulation described herein includes (a) obtaining paliperidone palmitate in micronized form; (b) adding the micronized

> paliperidone palmitate to a liquid medium to form a premix; and (c) subjecting the premix to mechanical means in the presence of a grinding medium to reduce the effective average particle size.

PTX-1 at 11:23-29.

253. The 693 Patent also discloses: the preferred procedure for adding the surface modifier to the premix, including the concentration of the surface modifier, PTX-1 at 11:50-56; the types of mills that can be used as mechanical means to grind down the particles, PTX-1 at 12:1-6; the preferred grinding media, as well as its density and composition, PTX-1 at 12:24-26; the specific order of steps for adding the premix, PTX-1 at 11:59-61; and the processing temperatures, PTX-1 at 12:34-35. *See* Tr. 979:11-980:19 (Little).

254. The 693 Patent provides detailed information about the ingredients, concentrations, particle sizes, and manufacturing of PP1M and PP3M, most of which Dr. Forrest ignored in giving his opinion on enablement. *See, e.g.*, Tr. 965:9-11 (Little) (regarding PTX-1 at 13:62-14:3), 969:22-24 (Little) (regarding PTX-1 at 4:33-39, 13:50-56); Tr. 980:20-22 (Little) (regarding manufacturing information).

d. Exemplary Formulations

255. In addition to the recipes for PP1M and PP3M, the 693 Patent contains "preferred" examples of the formulations with "specific inactive ingredients" and concentrations. Tr. 969:5-8, 967:7-968:1, 982:21-983:8 (Little).

256. For example, the 693 Patent provides that "[m]ost preferably, the inactive ingredients in the 3-month formulation will be polysorbate 20 (about 10

mg/mL), polyethylene glycol 4000 (about 75 mg/mL), citric acid monohydrate (about 7.5 mg/mL), sodium dihydrogen phosphate monohydrate (about 6 mg/mL), sodium hydroxide (about 5.4 mg/mL) and water for injection." PTX-1 at 13:56-62.

257. It adds that for "3-month paliperidone palmitate extended-release injectable suspension is preferably provided in a prefilled syringe (cyclic-olefin copolymer) prefilled with either 175 mg eq. (0.875 mL), 263 mg eq. (1.315 mL), 350 mg eq. (1.75 mL), or 525 mg eq. (2.625 mL) paliperidone (as 273 mg, 410 mg, 546 mg, or 819 mg paliperidone palmitate) suspension." PTX-1 at 4:33-39. As Dr. Little explained, this additional information in the 693 Patent specification "even lays out to a person of ordinary skill what concentration of that formulation to put into the syringe." Tr. 969:12-21 (Little).

258. Additionally, the 693 Patent discloses Invega Sustenna as an example of PP1M and Invega Trinza as an example of PP3M. *See* PTX-1 at 4:18-19, 5:23-24, 5:44-46, and 6:63-65 (Invega Sustenna); PTX-1 at 5:42-47 (Invega Trinza). Dr. Forrest is simply incorrect that there are "no working examples" of PP1M or PP3M. Tr. 982:21-983:8 (Little).

2. The Terms PP1M and PP3M Are Not Unduly Broad

259. Dr. Little and Dr. Forrest agree that PP1M and PP3M are described by their structural features in the 693 Patent (including ingredients, concentrations, and particle size) and are limited to the formulations with those structural features. Tr.

962:21-963:4 (Little) (describing structural features as recipes for PP1M and PP3M); Tr. 517:1-6 (Forrest) ("you have to go to the specification to understand what a PP1M and what a PP3M encompasses"); *see also* Tr. 518:3-8 (Forrest); Tr. 757:4-8 (Forrest).

260. Nevertheless, Dr. Forrest contends that the terms PP1M and PP3M encompass "well over 10 million possible combinations" because the structural features include "broad" particle size ranges and "long list[s]" of possible excipients. Tr. 518:3-12; Tr. 520:3-14 (Forrest).

261. However, as Dr. Little explained, a POSA would not view the 693 Patent's disclosure about PP1M and PP3M in a combinatorial fashion or as encompassing 10 million individual formulations. Tr. 980:23-981:6 (Little). It is standard to describe individual formulations using ranges for particle sizes or ingredients. *See* Tr. 1030:23-1031:5 (Little) ("**Q.** When you talk about one formulation from the perspective of a POSA, fair to say that that could include a particle size range and ranges of certain ingredients? **A.** Yes. **Q.** And that would be considered a formulation from the perspective of a [POSA]? **A.** It can be. And in the context of the patent, I think it is."). Dr. Little also testified that even if a POSA viewed the scope of the Asserted Claims as encompassing "thousands or millions of formulations," a POSA would "be able to make any one of those formulations . . . without undue experimentation." Tr. 982:8-14 (Little).

a. Excipients

262. Formulations typically contain inactive ingredients or excipients that help provide the correct dosage form for the active ingredient, which provides the pharmacological effect. Tr. 959:14-960:4 (Little). Wetting agents, buffers, and suspending agents are all classes of excipients included in PP1M and PP3M formulations. Tr. 965:14-23 (Little). The 693 Patent contains lists of suitable excipients for each class, as well as preferred excipients and concentrations. FOF 249; FOF 255-256 .

263. Dr. Forrest opined that because the Asserted Claims do not specify a single excipient to be used in PP1M and PP3M, the terms are "very broad" and could encompass "any combination" of the excipients listed in the 693 Patent specification. Tr. 521:2-10 (Forrest). For example, PP1M and PP3M require a surface modifier, and Dr. Forrest points to what he describes as a "long list of surface modifiers" in the 693 Patent, any of which could be used. Tr. 519:23-520:7, Tr. 521:2-10 (Forrest).

264. Again, Dr. Forrest fails to consider the disclosure of the 693 Patent from the perspective of a POSA. A POSA understands that if a formulation requires a wetting agent, it needs "something to perform that wetting function" and a POSA "would be able to select something from the list using information not only in the specification but also that they have available to them." Tr. 981:3-15 (Little).

Changing or trying different wetting agents is something that a POSA could do without undue experimentation. Tr. 968:5-20 (Little). Dr. Forrest also fails to recognize that the 693 Patent discloses preferred excipients and concentrations; for instance, polysorbate 20 is the preferred wetting agent, polyethylene glycol 4000 is the preferred suspending agent, and so on. PTX-1 at 14:9-13; 13:56-62; Tr. 967:16-968:1 (Little).

265. A POSA would be familiar with the classes of excipients used in PP1M and PP3M, as they are "taught this in their education and they know from their experience what the[ese] class[es] of excipients are and what they do" as well as the "amount that you would use." Tr. 965:14-21, 966:12-20. (Little). As Dr. Little explained, unitary formulations can be described using concentrations ranges for ingredients (or particle size ranges). Tr. 1030:23-1031:5 (Little)

266. As for the "long list[s]" of excipients in the 693 Patent, Dr. Little and Dr. Forrest ***agree*** that there is nothing unusual about such lists. Dr. Little testified that they are "very common," Tr. 967:5-6 (Little), and Dr. Forrest agreed that they are "commonly used" in patents, Tr. 759:13-15 (Forrest). In fact, as one example of this standard practice, one of Dr. Forrest's own patents has a list of pharmaceutical carriers that included 50 possible pharmaceutical carriers as well as derivatives and equivalents thereof. Tr. 759:16-760:7 (Forrest).

b. Particle size

267. Dr. Forrest also opined that the particle size ranges provided for PP1M and PP3M in the 693 Patent are "very broad." Tr. 519:3-15 (Forrest). When asked to "explain to the Court why [he] believe[s] those ranges to be broad," he stated only that there was a six-fold difference in the range for PP3M, and about a 20-fold difference for PP1M. *Id.* Dr. Forrest provides no other support for this conclusion, which is undercut by the fact that one of his own patents claims particle size ranges with a 10,000-fold difference, Tr. 761:4-8 (Forrest), much larger than the ranges in the 693 Patent that he calls "very broad."

268. Moreover, Dr. Little and Dr. Forrest agree that it is standard practice to describe particle size as a range. Dr. Forrest testified that it is "very hard to make particles that are all just one size because [POSAs] start with bigger particles" and "grind them down" resulting in "a range" of particle sizes. Tr. 420:2-12 (Forrest). Dr. Little agreed that, by their nature, particles exist as a size distribution such that it is "very common to refer to particle size as a range." Tr. 961:7-15 (Little). It is difficult, if not impossible, to recreate the exact same distribution of particle sizes between batches, and as a result, "it's very important to report them in terms of a range of particle sizes." Tr. 972:2-16 (Little).

269. Mylan's submissions to the FDA about its PP3M product illustrates this practice. [redacted]

[redacted] Notably, Dr. Forrest did not consider the particle size range Mylan submitted to the FDA for its PP3M product in rendering his opinion. Tr. 765:8-13 (Forrest).

271. Once Mylan's proposed parameters are accepted by the FDA, *i.e.*, "once a specification is ultimately set and approved," formulators going forward are "***going to trust the range is a PP3M formulation***." Tr. 976:13-977:1 (Little). In the same way, the inventors of the 693 Patent disclosed ranges for PP1M and PP3M in the 693 Patent thereby allowing a POSA to trust that "this is the formulation for PP1M and this is the formulation for PP3M." Tr. 973:10-13 (Little).

[22] Mylan's proposed acceptance criteria for its PP3M product included additional parameters or structural features of the formulation. Tr. 994:8-25 (Little).

272. As to the scope of the specific ranges for PP1M and PP3M, Dr. Little testified that in his experience, "these ranges are very reasonable and manageable to the person of ordinary skill in the art," even with the understanding that particle size can have an effect on the properties of a formulation. Tr. 972:17-22 (Little); Tr. 973:1-7 (Little).

c. Experimentation

273. Dr. Forrest testified repeatedly that the "different particle sizes and all the different excipients" for PP1M and PP3M would require "a lot of different experimentation to test all the possible combinations." Tr. 517:16-22 (Forrest); *see also, e.g.*, Tr. 518:9-15 (Forrest) ("[S]o you have to test all of those [combinations] to know . . . if you would be within what is a PP1M or a PP3M. That's a lot of experimentation."); Tr. 518:23-24 ("So it's a lot to test there."); Tr. 758:24-759:3 ("[Y]ou'd have to test many of those to know which would work if possible"). But Dr. Forrest did not proffer evidence that any experimentation is necessary to make and use PP1M and PP3M in the Asserted Claims.

274. As Dr. Little pointed out, Dr. Forrest "got it backwards" because the specification "gives a recipe to a person of ordinary skill in the art" such that a POSA would know they "have PP1M" and "have PP3M" by following that recipe; they would not have to test it to determine that. Tr. 981:19-982:5 (Little). Put another way, PP1M and PP3M are defined by their structural features, and a POSA

making the formulation with the described ingredients, concentrations, and particle sizes would know that they have PP1M or PP3M. Tr. 982:2-5 (Little) ("[The specification] gives a recipe to a person of ordinary skill in the art. So if you made it according to those things, you would have PP1M. If you made it according to the other things with PP3M, then you'd have PP3M.") In contrast, if the recipes were unknown, then "a person of ordinary skill in the art would have to figure all that out," for example, "the correct way to apply the dosage form . . . the kinds of ingredients . . . [and] what's important and what isn't." Tr. 960:5-17 (Little).

275. It is undisputed that changes to a formulation can, depending on the circumstances, affect its properties; for instance, changes to particle size can affect a formulation's pharmacokinetics. Tr. 848:15-19 (Gobburu); Tr. 1024:18-24 (Little); Tr. 973:1-5 (Little). That uncontroversial fact does not render the Asserted Claims non-enabled because the 693 Patent provides precise structural contours for the PP1M and PP3M formulations. The record is devoid of any evidence that variation ***within*** the structural contours disclosed by the 693 Patent would impact the properties of PP1M or PP3M in any meaningful way (*i.e.*, such that a POSA would need to do experimentation to make and use them in the Asserted Claims). Tr. 1024:18-24 (Little); Tr. 973:1-7 (Little).

276. Mylan's counsel incorrectly suggested that Dr. Gobburu had testified that changes within the PP1M and PP3M parameters would affect its

pharmacokinetics. *See* Tr. 1024:18-1025:1 (Little). In fact, Dr. Gobburu testified only to the general proposition that changes to a formulation ***can*** impact its pharmacokinetics; he did not testify at all about variations to PP1M or PP3M ***within*** the structural features and ranges identified in the 693 Patent. *See* Tr. 848:15-19, 854:14-855:3 (Gobburu). Moreover, Dr. Gobburu is neither an expert on formulations, nor an expert in how particle size or drug solubility would impact the bioavailability of a drug. Tr. 853:20-854:3 (Gobburu). He explained that for population PK modeling, "formulation characteristics . . . don't need to be included." Tr. 859:4-12 (Gobburu).

277. Thus, although Janssen's experts agree that changes to a formulation can result in changes to its properties, Mylan did not proffer any evidence that changes within the scope of PP1M and PP3M as defined in the 693 Patent result in changes to those formulations such that a POSA could not make and use the formulations of PP1M and PP3M in the claimed missed dose regimens.

3. Mylan Failed to Establish That Practicing the Full Scope of the Asserted Claims Would Require Undue Experimentation

278. Even accepting Dr. Forrest's contention that because of "the different particle sizes and all the different excipients" for PP1M and PP3M "it takes a lot of different experimentation to test all these possible combinations," he failed to specify ***what*** that testing would entail, how much time it would take, and whether or

not it was routine. Tr: 517:14-22, 518:3-15; 758:24-759:3 (Forrest). Mylan therefore failed to prove by clear and convincing evidence that the unspecified testing mentioned by Dr. Forrest rises to the level of undue experimentation.

279. Moreover, although Dr. Forrest opined that the 693 Patent does not provide sufficient information to practice the full scope of the terms "PP1M" and "PP3M," when asked ***seven times*** on cross-examination to identify a PP1M or PP3M formulation that was not enabled, Dr. Forrest could not identify any specific formulation or explain why it could not be made or used in the Asserted Claims. *See* Tr. 756:20-757:19, 758:2-9, 758:10-19, 765:15-19, 766:6-13, 766:14-767:6, 767:7-13 (Forrest). The most Dr. Forrest could do was refer to the 843 Patent, at one point suggesting it was "problematic" because it "included a formulation of a [one-]month depot that also overlapped with what the 693 [Patent] disclosed would be a three-month depot." Tr. 766:6-8, 767:1-6 (Forrest).

280. However, Dr. Forrest did not establish that the purportedly "problematic" formulation in the 843 Patent was either a PP1M or a PP3M formulation as described in the 693 Patent, or that it could not be made or used in the Asserted Claims—the relevant inquiry for enablement.[23] Tr. 766:6-8, 767:1-6

[23] Dr. Forrest vaguely suggests that the 843 Patent describes PP1M with a particle size of 5 µm. Tr. 522:17-20 (Forrest). However, the 843 Patent does not describe any formulations as PP1M or PP3M as used in the 693 Patent, DTX-3, and as both Dr. Little and Dr. Forrest agree, the 693 Patent unambiguously states that a

(Forrest).

281. The 843 Patent does not mention PP1M or PP3M as described in the 693 Patent (or missed dose dosing regimens). *See generally* DTX-3. Rather, the 843 Patent is incorporated by reference as background information in the 693 Patent, which ***does*** describe PP1M and PP3M. Tr. 766:9-13 (Forrest). Specifically, the 693 Patent incorporates the 843 Patent (and others) by reference to provide additional information about formulating pharmaceutical excipients and injectable dosage forms of paliperidones esters, and, as it states, "[s]uitable aqueous depot formulations." PTX-1 at 9:31-38; Tr. 970:16-971:4 (Little). To the extent a POSA relied on information from the 843 Patent to practice the 693 Patent, they would do so "through the lens" of the additional information in the 693 Patent. Tr. 1030:1-22 (Little). Thus, even if the examples in the 843 Patent were somehow "problematic," that would not prevent a POSA from making or using PP1M or PP3M, as those terms are described in the 693 Patent.

4. Dr. Forrest's Testimony on the State of the Prior Art Undercuts his Enablement Opinion

282. Dr. Forrest did not testify about the state of the prior art in discussing his enablement opinion. Tr. 522:1-4 (Forrest) (referring to state-of-the-prior-art and relative-skill-of-those-in-the-art *Wands* factors on Forrest Demonstratives Slide 72).

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paliperidone palmitate formulation of 5 μm is PP3M if it meets all the other PP3M parameters. Tr. 1020:15-19 (Little); Tr. 522:21-23 (Forrest).

283. However, in providing his obviousness opinion, Dr. Forrest testified that, based on the prior art, it would have been obvious to make and use PP1M and PP3M formulations in the claimed dosing regimen. Tr. 756:15-19 (Forrest). He testified that "a lot was known about paliperidone palmitate" in the prior art and in particular that "a lot was known about how you could control depot injections" even without the benefit of the recipe-like instructions of the 693 Patent. Tr. 411:23-412:10 (Forrest).[24]

284. Similarly, he testified that "particle size is one of the easiest ways" to "make a depot formulation and control how quickly it gets absorbed into the body." Tr. 406:19-407:3 (Forrest). He claimed that the relationship between changes to particle size and absorption was "well understood." Tr. 409:11-410:12 (Forrest). And he added that a "trick" used since his "days way back in school and before that too" was to "control" certain properties of a drug by "controlling the particle size." Tr. 401:1-5 (Forrest).

[24] Mylan may attempt to argue that Dr. Forrest's positions are not inconsistent because it is possible that "a" formulation of PP1M and "a" formulation of PP3M were obvious, but the entire scope of such formulations was not enabled. This tact was previewed in Dr. Little's cross-examination when he was asked whether "[w]hat Dr. Forrest was trying to say was that the prior art teaches us a Sustenna formulation and it would be obvious to create a PP3M formulation, but that the prior art doesn't teach multiple different formulations apart from Sustenna, right?" Tr. 995:22-25. But Dr. Forrest's testimony on obviousness was not so limited; Dr. Forrest testified generally that PP1M and PP3M formulations would have been obvious based on the prior art, not that any single identifiable formulation would have been obvious. Tr. 754:22-756:19 (Forrest); Tr. 996:11-21 (Little).

285. Although Dr. Forrest is incorrect, his testimony on the state of the prior art undermines his opinion that a POSA would not have been able to make and use PP1M and PP3M with the additional information provided by the 693 Patent.

C. MYLAN FAILED TO ESTABLISH THAT THE ASSERTED CLAIMS LACK WRITTEN DESCRIPTION

286. Mylan failed to establish that the Asserted Claims lack written description. The Asserted Claims are directed to missed dose dosing regimens and Dr. Forrest did not dispute that the 693 Patent provides an adequate written description of the claimed dosing regimens. Tr. 522:5-20 (Forrest); Tr. 985:4-9 (Little); *see also* PTX-1 at 2:33-3:5; 6:26-50; 18:20-33; 19:64-20:13.

287. Like his enablement opinion, Dr. Forrest's cursory written description opinion was focused on the claim terms "PP1M" and "PP3M" and was offered in the alternative to his obviousness opinion. Tr. 516:1-8, 522:8-20 (Forrest). The entirety of Dr. Forrest's opinion on written description at trial was less than 20 lines of testimony (including his description of the legal standard). *See* Tr. 522:5-523:9 (Forrest). Dr. Forrest testified that his written description opinion was based on his view that there are "no working examples of a PP3M" and "no structural features of a PP1M or a PP3M," and that the inventors therefore "don't show they possess the entire claimed range." Tr. 522:13-20 (Forrest). He added that the 693 Patent incorporates art, such as the 843 Patent that "describes a PP1M that's five microns

that falls right in the range of what they claimed for PP3M." Tr. 522:20-23 (Forrest).

288. Dr. Forrest's brief testimony fails to satisfy Mylan's burden to prove by clear and convincing evidence that the Asserted Claims are invalid for lack of written description. The 693 Patent specification provides extensive information about the structural features of PP1M and PP3M including: ingredients, concentrations, particle size, and manufacturing information. FOF 247-254. The specification also provides preferred examples of PP1M and PP3M as well as commercial embodiments. FOF 255-258. Dr. Little testified credibly that based on the specification's disclosure, it was "very clear that the inventors possessed what was a PP1M formulation and PP3M formulation" within the meaning of the Asserted Claims. Tr. 985:10-24 (Little).

289. As to the alleged inconsistencies between the 843 Patent and the 693 Patent, for the reasons described above, Dr. Forrest is incorrect. FOF 279-281. The 843 is incorporated by reference in the 693 Patent to provide background information about paliperidone ester formulations. FOF 281. A POSA would rely on the disclosure of the 693 Patent to understand the claimed inventions and to determine whether the inventors possessed those inventions.

PROPOSED CONCLUSIONS OF LAW

I. JURISDICTION AND STANDING

290. This Court has jurisdiction over the subject matter of this action pursuant to 28 U.S.C. §§ 1331 and 1338(a). "No party has contested personal jurisdiction or venue." FPTO at 1-2.

291. JPN and JPI have standing to bring this suit. FOF 3; *Schwendimann v. Arkwright Advanced Coating, Inc.*, 959 F.3d 1065, 1072 (Fed. Cir. 2020); *see, e.g.*, *In re Solodyn (Minocycline Hydrochloride) Antitrust Litig.*, No. 14-cv-2503, 2015 WL 5458570, at *2 (D. Mass. Sept. 16, 2015).

II. MYLAN INDUCES INFRINGEMENT

292. A patentee must prove infringement by a preponderance of the evidence. *Vanda Pharm. Inc. v. West-Ward Pharm. Int'l Ltd.*, 887 F.3d 1117, 1125 (Fed. Cir. 2018). Here, Janssen has met its burden.

293. It is "an act of [patent] infringement to submit . . . an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act [codified at 21 U.S.C. § 355(j),] . . . for a drug claimed in a patent or the use of which is claimed in a patent, . . . if the purpose of such submission is to obtain approval under such Act to engage in the commercial manufacture, use, or sale of a drug . . . claimed in a patent or the use of which is claimed in a patent." 35 U.S.C. § 271(e)(2). Analyzing infringement under this provision "is focused on a comparison of the

asserted patent claims against the product that is likely to be sold following ANDA approval." *Vanda*, 887 F.3d at 1125 (cleaned up).

294. Janssen contends that Mylan's Proposed Labels will induce infringement of the Asserted Claims. "Whoever actively induces infringement of a patent shall be liable as an infringer." 35 U.S.C. § 271(b). To prevail on a theory of induced infringement, a plaintiff must prove (1) direct infringement and (2) that the defendant had the specific intent to induce infringement. *Vanda*, 887 F.3d at 1129.

A. Healthcare Providers Following Mylan's Proposed Labels Will Directly Infringe the Asserted Claims

1. Mylan's Proposed Labels Recite Every Element of the Asserted Claims

295. In assessing infringement of method-of-treatment claims in the Hatch-Waxman context, "courts compare[] the wording of the [proposed drug] label to the patent claims." *BTG Int'l Ltd. v. Amneal Pharm. LLC*, 352 F. Supp. 3d 352, 394-95 (D.N.J. 2018), *appeal dismissed in relevant part as moot*, 923 F.3d 1063, 1077 (Fed. Cir. 2019). Proposed drug labels "encompass infringement" if the "label meets the claim limitations of the patent" or the "label language aligns with the language of [the Asserted Claims]." *Id.*; *see also GlaxoSmithKline LLC v. Teva Pharm. USA, Inc.*, 7 F.4th 1320, 1330 (2021) (finding substantial evidence to support jury's determination that label encouraged each claimed step where expert

"marched through [the] label explaining how it met the limitations of [the] claim"), *reh'g and reh'g en banc denied*, 25 F.4th 949 (Fed. Cir. 2022), *petition for cert. pending*, No. 22-37 (filed July 11, 2022).

296. Here, it is undisputed that Mylan's Proposed Labels meet every element of the Asserted Claims. FOF 49-50; *see also* FOF 51-62.

2. A Single Actor, a Healthcare Provider, Will Perform All Steps of the Claimed Dosing Regimens

297. Direct infringement "occurs where all steps of a claimed method are performed by or attributable to a single entity." *Akamai Techs., Inc. v. Limelight Networks*, 797 F.3d 1020, 1022 (Fed. Cir. 2015) (en banc). "Divided infringement" refers to the situation where "no single actor performs all ***steps*** of a method claim." *Eli Lilly & Co. v. Teva Parenteral Meds., Inc.*, 845 F.3d 1357, 1364 (Fed. Cir. 2017). When the steps of the method are divided among multiple actors, the claimed method is infringed only if "the acts of one are attributable to the other such that a single entity is responsible for the infringement." *Id.*

298. Method-of-treatment claims typically set forth requirements as to the patient population that are not themselves steps of a claimed method. *See, e.g.*, *Pernix Ireland Pain DAC v. Alvogen Malta Operations Ltd.*, 323 F. Supp. 3d 566, 576 (D. Del. 2018) (Bryson, C.J., sitting by designation), *aff'd sub nom. Persion Pharm. LLC v. Alvogen Malta Operations Ltd.*, 945 F.3d 1184 (Fed. Cir. 2019) (steps of a claimed "method of treating pain in a patient having mild or moderate

hepatic impairment" did not include patient getting mild or moderate hepatic impairment); *see also* Tr. 28:12-22, 33:9-17 (Mylan's counsel).

a. The Claimed Dosing Regimens Have Three Steps

299. When interpreting the meaning of patent claims, courts "start with the claim language." *Straight Path IP Grp., Inc. v. Sipnet EU S.R.O.*, 806 F.3d 1356, 1360 (Fed. Cir. 2015); *Facebook, Inc. v. Pragmatus AV, LLC*, 285 F. App'x 864, 867 (Fed. Cir. 2014) ("We start with the language of the claims themselves."); *800 Adept, Inc. v. Murex Sec., Ltd.*, 539 F.3d 1354, 1363 (Fed. Cir. 2008) ("As usual, we start with the language of the claims themselves."); *see Phillips v. AWH Corp.*, 415 F.3d 1303, 1314 (Fed. Cir. 2005) (en banc) ("Quite apart from the written description and the prosecution history, the claims themselves provide substantial guidance as to the meaning of a particular claim term.").

300. Here, the language of the claims makes it clear that the claimed dosing regimens have three steps, consisting of the three numbered reinitiation doses. FOF 67-77. Where, as here, claim language is clear, "leaving no genuine uncertainties on interpretive questions relevant to the case, it is particularly difficult to conclude that the specification reasonably supports a different meaning." *Straight Path*, 806 F.3d at 1361. In such situations, "[t]he specification plays a more limited role than in the common situation where claim terms are uncertain in meaning in relevant respects." *Id.*; *accord Trs. of Columbia Univ. v. Symantec*

Corp., 811 F.3d 1359, 1364 n.2 (Fed. Cir. 2016) ("Absent implied or explicit lexicography or disavowal, we have recognized that the specification plays a more limited role where claim language has so plain a meaning on an issue that it leaves no genuine uncertainties on interpretive questions relevant to the case.") (alteration and internal quotation marks omitted).

301. Although having "been last administered a PP3M injection 4 to 9 months ago" is a requirement of the Asserted Claims, it is not a step of the claimed dosing regimens. *See, e.g., Orexigen Therapeutics, Inc. v. Actavis Lab'ys, FL, Inc.*, 282 F. Supp. 3d 793, 798 (D. Del. 2017) (holding that the act of diagnosing obesity is not a step of a claimed method of treating obesity "comprising administering [a pair of compounds] to an individual who has been diagnosed as suffering from overweight or obesity"); *In re Biogen '755 Patent Litigation*, No. 10-cv-2734 (CCC)(JBC), 2016 WL 7340311, at *5-9 (D.N.J. Mar. 28, 2016) (finding claim terms "produced by" and "transformed by" were not steps of claimed method because they conveyed action that "'***must have been'*** done rather than what '***must be'*** done).[25]

[25] *Cf. Core Wireless Licensing S.A.R.L. v. Apple, Inc.*, No. 15-cv-5008, 2016 WL 6427850, at *4-5 (N.D. Cal. Oct. 31, 2016) (relying on "grammar and indentation" of the claim to distinguish the claimed steps, which "each start on a separate line with a gerund . . . demonstrating how the method should be performed," from other claim limitations, which "describe the environment in which the method . . . is practiced"); *AMAG Pharm., Inc. v. Sandoz, Inc.*, No. 16-cv-1508 (PGS), 2017 WL 3076974, at *25 (D.N.J. July 19, 2017) (Method steps "should usually be verbal

302. The "the plainness of the claim language necessarily affects what ultimate conclusions about claim construction can properly be drawn based on the specification." *Straight Path*, 806 F.3d at 1361. Because the language of the Asserted Claims is clear, the intrinsic evidence "plays a more limited role" in claim interpretation than it does when the language is ambiguous. *Trs. of Columbia Univ.*, 811 F.3d at 1364 n.2.

303. In any event, the specification and the prosecution history are entirely consistent with the conclusion that the dosing regimens of the Asserted Claims have three steps. FOF 78.

304. The claimed dosing regimens have three steps, consisting of administering the three reinitiation doses numbered "(1)," "(2)," and "(3)" of the Asserted Claims.

b. Healthcare Providers Will Perform Each of the Three Steps of the Claimed Dosing Regimens and Directly Infringe the Asserted Claims

305. It is undisputed that HCPs using Mylan's proposed generic products will administer each of the three reinitiation doses of the Asserted Claims to the patient population identified by the Asserted Claims. FOF 88-90. Accordingly, HCPs will directly infringe the Asserted Claims.

(gerundial) phrase[s], introduced by a gerund or verbal noun (the '-ing' form of a verb)."

B. Mylan Specifically Intends to Induce Infringement

306. Induced infringement in an ANDA case requires showing that the proposed labels "encourage, recommend, or promote infringement." *Vanda*, 887 F.3d at 1129. Proposed labels induce infringement if they either "[(1)] implicitly or explicitly encourage or [(2)] instruct users to take action that would inevitably lead to [use of a drug in an infringing way]." *See GlaxoSmithKline*, 7 F.4th at 1330 (cleaned up).

1. The Explicit Instructions in Mylan's Proposed Labels Establish Specific Intent to Induce Infringement

307. In deciding induced infringement, "courts compare[] the wording of the [proposed drug] label to the patent claims." *BTG*, 352 F. Supp. 3d at 394-95. Proposed drug labels "encompass infringement" if the "label meets the claim limitations of the patent" or the "label language aligns with the language of [the Asserted Claims]." *Id.*; *see also GlaxoSmithKline*, 7 F.4th at 1330.

308. "[W]hether the Court makes such an inference [of specific intent] depends on how explicitly the instructions suggest the infringement." *Acorda Therapeutics Inc. v. Apotex Inc.*, No. 07-cv-4937 (GEB)(MCA), 2011 WL 4074116, at *17 (D.N.J. Sept. 6, 2011), *aff'd*, 476 F. App'x 746 (Fed. Cir. 2012). "Depending on the clarity of the instructions, the decision to continue seeking FDA approval of those instructions may be sufficient evidence of specific intent to induce infringement." *Eli Lilly*, 845 F.3d at 1368.

309. In an ANDA case, "[p]roposed labeling that instructs [an] infringing use[] is generally sufficient to support a finding of intentional inducement." *BTG*, 352 F. Supp. 3d at 399 (collecting cases); *see also GlaxoSmithKline LLC v. Glenmark Generics Inc., USA*, No. 14-cv-877, 2015 WL 3793757, at *6 (D. Del. Apr. 22, 2015) ("[T]here is no question that statements in a package insert that encourage infringing use of a drug product are alone sufficient to establish intent to encourage direct infringement for purposes of an induced infringement claim.") (internal quotation marks omitted).

310. Mylan's Proposed Labels explicitly instruct HCPs to reinitiate patients onto PP3M in an infringing manner. FOF 91-92. The express instructions on Mylan's Proposed Labels are sufficient evidence of induced infringement. *See BTG*, 352 F. Supp. 3d at 399.

2. The Fact That Mylan's Proposed Labels Will Inevitably Lead to Infringement Establishes Specific Intent to Induce Infringement

311. "[E]vidence that the product labeling that [Mylan] seek[s] would inevitably lead some [HCPs] to infringe establishes the requisite intent for inducement." *Eli Lilly*, 845 F.3d at 1369. An ANDA applicant has "the requisite specific intent to induce infringement" when it "include[s] instructions in its proposed label that will cause at least some users to infringe the asserted method claims." *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1060 (Fed. Cir. 2010);

accord Catalyst Pharm., Inc. v. Jacobus Pharm. Co., No. 20-cv-14590 (MAS)(DEA), 2021 WL 3293430, at *5 (D.N.J. July 31, 2021); *Impax Lab'ys, Inc. v. Actavis Lab'ys FL, Inc.*, No. 15-cv-6934 (SRC)(CLW), 2018 WL 1863826, at *13 (D.N.J. Apr. 18, 2018).

312. Missed doses are inevitable, [redacted] FOF 95-96. Patients will inevitably return for treatment four to nine months after their last dose. FOF 96-97. HCPs will inevitably follow the instructions of Mylan's Proposed Labels. FOF 97-98. HCPs following the instructions of Mylan's Proposed Labels will infringe the Asserted Claims. FOF 88-90. Thus, Mylan's Proposed Labels will inevitably lead some HCPs to infringe, thereby establishing Mylan's intent to induce infringement.

313. "[P]atentees in Hatch-Waxman litigations asserting method patents do not have to prove that prior use of the NDA-approved drug satisfies the limitations of the asserted claims." *Vanda*, 887 F.3d at 1130 (citing *Sanofi v. Watson Lab'ys Inc.*, 875 F.3d 636, 643 (Fed. Cir. 2017). Nonetheless, HCPs have reinitiated patients who had their last dose of Invega Trinza four to nine months ago according to the Invega Trinza label, further establishing induced infringement. FOF 97.

3. The Testimony of Mylan's Corporate Witness Establishes Mylan's Specific Intent to Induce Infringement

314. Testimony from a company witness is relevant to whether the company intends to induce infringement. *See GlaxoSmithKline*, 7 F.4th at 1333.

Testimony from Mylan's corporate witness further demonstrates Mylan's intent to induce infringement. FOF 99.

4. Mylan's Non-Infringement Arguments Fail

315. "For purposes of inducement, 'it is irrelevant that some users may ignore . . . the proposed label.'" *Eli Lilly*, 845 F.3d at 1368 (quoting *AstraZeneca*, 633 F.3d at 1060). As long as Mylan's Proposed Labels "instruct [HCPs] to follow the instructions in an infringing manner," the labels are "sufficient [to prove induced infringement] even though some users would not follow the instructions." *Id.* at 1368-69. The fact that Dr. Berger will not follow the label, or that some patients will not return for reinitiation treatment 4 to 9 months after their last dose of PP3M, is therefore irrelevant to infringement, given that Mylan's Proposed Labels instruct HCPs to practice the Asserted Claims and some will. FOF 94-98.

316. Evidence of substantial noninfringing uses does not preclude a finding of specific intent. *See Sanofi*, 875 F.3d at 646; *see also Vanda*, 887 F.3d at 1133 ("[E]ven if the proposed ANDA product has 'substantial noninfringing uses,' [the ANDA applicant] may still be held liable for induced infringement."); *Eli Lilly*, 845 F.3d at 1368-69 ("[A] label that instructed users to follow the instructions in an infringing manner was sufficient . . . even though the product in question had substantial noninfringing uses."). Even if Mylan's Proposed ANDA Products have noninfringing uses, Mylan's Proposed Labels nonetheless encourage, recommend,

or promote infringement because they instruct HCPs to infringe the Asserted Claims. FOF 100-102.

III. THE ASSERTED CLAIMS ARE PRESUMED VALID

317. Having been issued by the Patent Office, the Asserted Claims are presumed valid. 35 U.S.C. § 282(a); *Microsoft Corp. v. i4i Ltd. P'ship*, 564 U.S. 91, 110-14 (2011). To overcome this presumption, Mylan must prove invalidity "by clear and convincing evidence." *i4i*, 564 U.S. at 109-10.

318. At trial, Mylan relied on *i4i* to argue that because JAMA was not expressly cited to the PTO, the patent is not entitled to a presumption of validity. *See* Tr. 322:21-323:14. In *i4i*, the Supreme Court expressly ***rejected*** Microsoft's argument that obviousness should be determined by a preponderance-of-evidence standard rather than a clear-and-convincing standard "where the evidence before the factfinder was not before the PTO during the examination process." 564 U.S. at 108. The clear-and-convincing standard still applies. *Id.* at 109.

319. Although the Supreme Court suggested that it may be relevant whether prior art was before the PTO, *id.* at 110-11, the evidence at trial showed that the PTO conducted multiple literature searches that would have captured JAMA. FOF 21 n.3. Further, JAMA does not add "materially new" evidence, *see i4i*, 564 U.S. at 111, to the combination of PP1M and PP3M references already considered by the PTO—against which the claims were allowed—because, as Dr.

Forrest admitted, JAMA discloses none of the key elements described in paragraph 324 below. FOF 109. For example, Dr. Forrest admitted that JAMA does not disclose "using PP1M after a patient had been advanced to PP3M," or "giving PP3M without first stabilizing the patient on PP1M for at least a few months." *Id.* Although the PP3M reference cited by the PTO was Osborne rather than JAMA, its reasoning for allowing the patent constitutes a direct rejection of Mylan's obviousness arguments here. FOF 25, 83.

IV. MYLAN FAILED TO PROVE OBVIOUSNESS

320. Mylan has failed to establish, by clear and convincing evidence, that "the differences between the claimed invention and the prior art are such that the claimed invention ***as a whole*** would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art." 35 U.S.C. § 103; *see Sanofi-Synthelabo v. Apotex, Inc.*, 550 F.3d 1075, 1086 (Fed. Cir. 2008) ("The determination of obviousness is made with respect to the ***subject matter as a whole***, not separate pieces of the claims.").

321. Obviousness is a question of law based on underlying facts, including: (1) the scope and content of the prior art; (2) the differences between the claimed subject matter and the prior art; (3) the level of ordinary skill; and (4) objective indicia of nonobviousness. *See Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966). "All of the *Graham* factors must be considered, including the objective

indicia when present, before any conclusion regarding obviousness is reached." *Millennium Pharm., Inc. v. Sandoz, Inc.*, 862 F.3d 1356, 1367 (Fed. Cir. 2017).

322. "Obviousness cannot be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention." *Cheese Sys., Inc. v. Tetra Pak Cheese & Powder Sys., Inc.*, 725 F.3d 1341, 1352 (Fed. Cir. 2013) (internal quotation marks omitted). Moreover, an "invention is not obvious simply because all of the claimed limitations were known in the prior art at the time of the invention. Instead, we ask whether there is a ***reason, suggestion, or motivation*** in the prior art that would lead one of ordinary skill in the art to combine the references." *Forest Lab'ys, LLC v. Sigmapharm Lab'ys, LLC*, 918 F.3d 928, 934 (Fed. Cir. 2019) (internal quotation marks omitted).

323. To this end, a "party seeking to invalidate a patent based on obviousness must demonstrate by clear and convincing evidence that a skilled artisan would have had ***reason to combine*** the teaching of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a ***reasonable expectation of success*** from doing so." *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig.*, 676 F.3d 1063, 1068-69 (Fed. Cir. 2012) (internal quotation marks omitted). "The presence or absence of a motivation to combine" and "of a reasonable expectation of success" are questions

of fact. *See Novartis Pharms. Corp. v. West-Ward Pharms. Int'l Ltd.*, 923 F.3d 1051, 1059 (Fed. Cir. 2019) (internal quotation marks omitted).

A. Mylan Failed to Prove That Every Element of the Asserted Claims Was Known in the Prior Art

324. The Asserted Claims are a unique combination of elements that provide, among other things, (a) a missed dose regimen for PP3M, (b) administered to a specific patient population whose last dose of PP3M was 4-9 months ago, (c) treating the patient, who had been advanced from PP1M to PP3M, with PP1M reinitiation loading doses, and (d) returning the patient to maintenance treatment with PP3M without first stabilizing the patient on PP1M for several months. Tr. 538:2-20 (Sommi).

325. As challenger, Mylan had the "burden to prove that all claimed limitations are disclosed in the prior art." *Par Pharm. v. TWi Pharm., Inc.*, 773 F.3d 1186, 1194 (Fed. Cir. 2014); *accord Univ. of Strathclyde v. Clear-Vu Lighting LLC*, 17 F.4th 155, 160 (Fed. Cir. 2021). Mylan failed to meet that burden.

326. At trial, Dr. Forrest admitted that the prior art discloses none of the claim limitations described in paragraph 324. Tr. 684:18-20, 685:9-16, 686:2-14 (Forrest) ("**Q.** . . . In your direct testimony, did you identify any prior art reference as disclosing a ***missed dose regimen for PP3M***? **A.** No . . ."; "**Q.** In your direct testimony, did you identify any prior art reference as disclosing the ***four-to-nine-month target patient population***? **A.** Not directly."; "**Q.** In your direct testimony,

did you identify any prior art reference as disclosing ***using PP1M after a patient had been advanced to PP3M***? **A.** Not directly."; "**Q.** There was no reference—prior art reference—that you relied on in your direct as disclosing ***giving PP3M without first stabilizing the patient on PP1M for at least a few months***. Did I understand that correctly? **A.** Correct."); FOF 109. Neither the PP3M references (JAMA, the 2014 Press Release, and NCT 423) nor the PP1M references (Invega Sustenna Label, the 536 Publication, the 519 Publication and Samtani 2009) disclose or suggest these limitations. FOF 118, 120. The failure to identify any of these limitations in any prior art reference is fatal to Mylan's obviousness challenge.

327. The exception to the general rule requiring an obviousness challenger to identify all claim limitations in the prior art is where the "common knowledge" of a POSA is used to supply a missing limitation. *See Arendi S.A.R.L. v. Apple Inc.*, 832 F.3d 1355, 1361-62 (Fed. Cir. 2016). But that exception is applicable only in the rare circumstance where "the limitation in question [is] unusually simple and the technology particularly straightforward." *Id.* at 1362; *accord Koninklijke Philips NV v. Google LLC*, 948 F.3d 1330, 1338 (Fed. Cir. 2020). And even then, "references to 'common sense' . . . cannot be used as a wholesale substitute for reasoned analysis and evidentiary support." *Arendi*, 832 F.3d at 1362; *accord Koninklijke*, 948 F.3d at 1338.

328. Dr. Forrest did not testify that he was relying on "common sense" or "common knowledge" to supply missing claim limitations. Rather he relied on prior art references. *See, e.g.*, Tr. 474:7-475:15 (Forrest); Forrest Demonstratives Slide 6 ("The prior art renders obvious the asserted claims of the '693 patent based on JAMA in view of the '536 publication, the '519 publication, and Invega Sustenna label."); *id.* at Slide 43 ("The Approach to Missed Doses for PP3M Was Taught by the Prior Art."). The phrases "common sense" or "common knowledge" were not uttered even once at trial. Furthermore, "common sense" cannot be used to supply missing elements in this case because the missing elements are not "unusually simple" and the technology at issue is not "particularly straightforward." FOF 167-168; *see Arendi*, 832 F.3d at 1362; *Sanofi-Aventis Deutschland GmbH v. Glenmark Pharm. Inc., USA*, 748 F.3d 1354, 1360 (Fed. Cir. 2014) ("[I]n the medical arts potential solutions are less likely to be genuinely predictable, as compared with other arts such as the mechanical devices in *KSR*.") (cleaned up).

329. To the extent Mylan relies on Dr. Forrest's vague resort to knowledge of a POSA, "routine optimization," or other similarly vague testimony to supply the missing claim limitations, FOF 196 & n.18, that testimony lacks the requisite "reasoned analysis" and "evidentiary support" the law demands before invoking the "common sense" exception to the general rule requiring an obviousness challenger

to identify all claim limitations in the prior art. *See Arendi*, 832 F.3d at 1362; *accord Koninklijke*, 948 F.3d at 1338.

330. Because it failed to show that all elements of Asserted Claims are disclosed in the prior art or that the common knowledge of a POSA could have supplied these elements, Mylan has failed to prove obviousness.

B. Mylan Failed to Prove a Motivation to Combine the Prior Art to Arrive at the Asserted Claims with a Reasonable Expectation of Success

331. Even if Mylan had proved that the missing elements were somehow disclosed in the prior art, Mylan failed to prove by clear and convincing evidence that a POSA would have had a motivation or reason to combine the elements of the claimed dosing regimen in the manner claimed to arrive at the Asserted Claims with a reasonable expectation of success. *See Cyclobenzaprine*, 676 F.3d at 1068-69.

332. Even before considering the specific deficiencies in the testimony of Mylan's obviousness expert, Dr. Forrest, the testimony of Mylan's clinical expert, Dr. Berger, affirmatively dooms Mylan's obviousness case. Dr. Berger testified, repeatedly and without qualification, that, at relevant time (*i.e.*, the effective filing date of the 693 Patent), a POSA such as himself would have considered the dosing regimen of the Asserted Claims for PP3M patients who had missed a dose to be "a bad idea," "unsafe," "unreasonable," and "unwise." FOF 194. A POSA would have had no motivation or reason to arrive at a dosing regimen, and no reasonable

expectation of success in using a dosing regimen, that is "unsafe," "unreasonable," or "unwise." Mylan's own expert provided affirmative evidence that defeats any conclusion that the Asserted Claims would have been obvious. *See, e.g.*, *Nichia Corp. v. Everlight Ams., Inc.*, 855 F.3d 1328, 1337 (Fed. Cir. 2017) (patent challenger's own 30(b)(6) witness's "admission that electronic device technology is not particularly relevant to LED technology" was given "weight" and supported "no motivation to combine these references" that teach different technologies); *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1358-60 (Fed. Cir. 2007) (patent challenger's own 30(b)(6) witness's admission that the purported lead compound "had the negative side effects" and its expert's admission that it is "undesirable" "buttressed" the challenger's failure to prove obviousness).

1. No Motivation to Treat the 4-9 Month Patient Population with a Reasonable Expectation of Success

333. Mylan failed to prove by clear and convincing evidence that a POSA would have had a reason or motivation to combine the teachings of the prior art references, with a reasonable expectation of success, to identify for treatment the claimed target patient population, namely those who had been treated with PP3M and whose last dose was 4-9 months ago.

334. Dr. Forrest presented several different theories on this point, none of which were applied consistently or with scientific rigor: (1) the Invega Sustenna label extrapolation theory; (2) the 4-5 half-life extrapolation theory; (3) the

unfounded interpretation of interim data reported in JAMA; and (4) his unscientific PK modeling. FOF 119-180. A POSA would have had no motivation or reasonable expectation of success of using any these theories.

335. Dr. Forrest relied on the Invega Sustenna Label extrapolation theory to identify the 4-month front end (but not the back end) of the intermediate window, and he relied on an amalgam of the other theories to identify the 9-month back end (but not the front end) of the intermediate window. FOF 122, 128, 140, 177. Dr. Forrest's results-oriented cherry-picking approach demonstrates that he relied on impermissible hindsight, violating "the longstanding principle that the prior art must be considered for all its teachings, not selectively." *Henny Penny Corp. v. Frymaster LLC*, 938 F.3d 1324, 1332 (Fed. Cir. 2019).

336. As for Dr. Forrest's PK modeling, it was based on assumptions and extrapolations that were unscientific. FOF 152-176. Dr. Forrest's modeling ignored known characteristics of paliperidone palmitate, and the model failed to describe the initial rise of plasma concentrations, failed to predict the actual PK properties of PP1M and PP3M, and yielded PK assumptions that were inconsistent with the prior art on which Dr. Forrest relied as well as with Dr. Forrest's other theories. FOF 152-176. As a result, Mylan failed to establish by clear and convincing evidence that a POSA would have had a reason to use, and a reasonable

expectation of success in using, Dr. Forrest's PK modeling approach to come up with a missed dose dosing regimen for PP3M.

337. A POSA attempting to develop a PP3M missed dose regimen, and considering Dr. Forrest's theories for identifying the claimed 4-9 month patient population, "would have been faced, at best, with an array of inconclusive and sometimes contradictory teachings," and would not have had a motivation or reasonable expectation of success in treating the specific patient population. *Merck Sharp & Dohme Corp. v. Hospira Inc.*, No. 14-cv-915, 2016 WL 5872620, at *7 (D. Del. July 10, 2016).

2. No Motivation to Treat a Patient Who Had Been Successfully Advanced to PP3M Using PP1M with a Reasonable Expectation of Success

338. Mylan failed to prove by clear and convincing evidence that a POSA would have had a reason to combine the teachings of the prior art references, with a reasonable expectation of success, to use PP1M to treat a patient who had been successfully advanced to PP3M and then returned for treatment 4-9 months later. The prior art provides no reason, suggestion, or motivation to revert to PP1M after a patient has advanced to PP3M and missed a dose of PP3M. FOF 191-204.

339. Dr. Forrest relied on the unsupported assertion that "it was known that PP1M could be used to load them up with drug pretty rapidly" as a purported rationale for why a POSA would be motivated to reinitiate using PP1M rather than

PP3M (or anything else).[26] FOF 195. To the extent this is a reference to "common sense" or general knowledge, that "cannot be used as a wholesale substitute for reasoned analysis and evidentiary support." *See Arendi*, 832 F.3d at 1362.

340. Contrary to Dr. Forrest's unsupported opinion, the credible evidence of record demonstrates that, since the prior art lacked PK data for PP3M, a POSA would not have had any reason to know or predict whether PP1M would be any faster than PP3M at loading the patients up, let alone have a reasonable expectation of success in doing so. FOF 196-97; *see Grünenthal GmbH v. Alkem Lab'ys Ltd.*, 919 F.3d 1333, 1344 (Fed. Cir. 2019) (no reasonable expectation of success where art not "reasonably predictable"); *Honeywell Int'l, Inc. v. Mexichem Amanco Holding S.A. De C.V.*, 865 F.3d 1348, 1354 (Fed. Cir. 2017) ("evidence showing unpredictability in the art" indicates that a POSA "would not have been motivated to combine the references with a reasonable expectation of success").

341. Indeed, to the extent a POSA would utilize Dr. Forrest's approach at all, Dr. Forrest's own PK modeling suggests that PP3M reaches therapeutic levels

[26] Dr. Forrest's opinion was only that PP1M "could" be used. The "'mere fact that the prior art ***could*** be so modified would not have made the modification obvious unless the prior art suggested the ***desirability*** of the modification.'" *Orexo AB v. Actavis Elizabeth LLC*, 903 F.3d 1265, 1272-73 (Fed. Cir. 2018) (quoting *In re Gordon*, 733 F.2d 900, 902 (Fed. Cir. 1984)); *Belden Inc. v. Berk-Tec LLC*, 805 F.3d 1064, 1073 (Fed. Cir. 2015) ("[O]bviousness concerns whether a skilled artisan not only ***could have made*** but ***would have been motivated to make*** the combinations or modifications of prior art to arrive at the claimed invention.") (emphases in original).

at the same rate, if not faster than PP1M. FOF 199-202. Accordingly, the sole motivation on which Dr. Forrest relied to suggest that a POSA would have reinitiated with PP1M is contradicted by his own PK modeling exercise. Likewise, Mylan's own clinical expert, Dr. Berger, testified that "before Invega Trinza came out," it would have been "far safer" and "far wiser" to reinitiate nonadherent patients using PP3M.[27] FOF 194. Mylan not only failed to prove that a POSA would have been motivated to use PP1M to reinitiate PP3M patients, but it actually presented affirmative evidence, in the form of Dr. Forrest's modeling and Dr. Berger's testimony, that a POSA would not have had such a motivation. *See, e.g.*, *Nichia Corp.*, 855 F.3d at 1337; *Takeda*, 492 F.3d at 1358-60.

3. No Motivation to Use PP3M Without Stabilizing with Four or More Months of PP1M with a Reasonable Expectation of Success

342. Mylan also failed to prove by clear and convincing evidence that a POSA would have had a reason to combine the teachings of the prior art references, with a reasonable expectation of success, to return a patient to PP3M treatment

[27] The testimony of Dr. Berger and Dr. Sommi—both of whom have extensive clinical experience with antipsychotics—on the clinical motivations of a POSA carry far more weight than the testimony of Dr. Forrest. *See, e.g.*, *Asetek Danmark A/S v. CMI USA, Inc.*, 100 F. Supp. 3d 871, 886 & n.5 (N.D. Cal. 2015) (the testimony of expert who had "significantly more firsthand experience in [the] particular technology" was "entitled to greater weight" in determining nonobviousness), *aff'd on other grounds*, 852 F.3d 1352 (Fed. Cir. 2017); *Ultratec, Inc. v. Sorenson Commc'ns, Inc.*, 733 F. App'x 535, 539 (Fed. Cir. 2018) (it was "reasonable for the jury to reject" the testimony of an expert "because he lacked familiarity with the relevant field.").

without first stabilizing that patient on PP1M for several months. The prior art does not provide any reason, suggestion or motivation on this point, nor did Dr. Forrest even attempt to articulate such a rationale (except using hindsight). FOF 182, 205. The failure to establish a reason or motivation is another reason why Mylan has failed to establish obviousness by clear and convincing evidence. *See Cyclobenzaprine*, 676 F.3d at 1068-69; *InTouch Techs., Inc. v. VGo Commc'ns, Inc.*, 751 F.3d 1327, 1351 (Fed. Cir. 2014) ("A reason for combining disparate prior art references is a critical component of an obviousness analysis; 'this analysis should be made explicit.'") (quoting *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007)). In light of the prior art teachings that required patients to be stabilized on PP1M for at least four months before advancing to PP3M, FOF 205, a POSA would not have been motivated to arrive at the claimed dosing regimen—requiring two and only two catch-up doses of PP1M before returning a patient to treatment with PP3M—let alone with a reasonable expectation of success in doing so.

C. Mylan Impermissibly Relied on Hindsight

343. "A factfinder should be aware . . . of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning." *KSR*, 550 U.S. at 421. Here, Mylan's obviousness case is built almost exclusively on impermissible hindsight. FOF 104-180. A hindsight-based obviousness challenge cannot invalidate a patent. *See Cheese Sys.*, 725 F.3d at 1352; *In re*

Fritch, 972 F.2d 1260, 1266 (Fed. Cir. 1992) ("It is impermissible to use the claimed invention as an instruction manual or 'template' to piece together the teachings of the prior art so that the claimed invention is rendered obvious."); *In re Fine*, 837 F.2d 1071, 1075 (Fed. Cir. 1988) ("One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.").

344. Mylan's obviousness expert, Dr. Forrest—who had no experience with antipsychotics or paliperidone prior to this case—was handed the references and specific obviousness combinations by Mylan's counsel when he was first retained, and signed his 189-page expert report on the subject a few weeks later. FOF 105-106. This is blatant evidence of hindsight. *See, e.g.*, *Warner Chilcott Lab'ys Ireland Ltd. v. Impax Lab'ys, Inc.*, No. 08-cv-6304 (WJM)(MF), 2012 WL 1551709, at *57 (D.N.J. Apr. 30, 2012) (finding impermissible hindsight when "Defendants' experts started with the [] Patent, picked and chose from the already-narrowed list of references that Defendants' lawyers provided, and worked backwards using improper hindsight"), *aff'd*, 478 F. App'x 672 (Fed. Cir. 2012).

345. Dr. Forrest further revealed his use of hindsight by not consistently applying any one theory in his attempts to identify ***both*** the front ***and*** the back end of the 4-9 month intermediate window, suggesting that he used the Asserted Claims in deriving these theories. FOF 119-151. Dr. Forrest's use of the Asserted Claims

to provide knowledge of the solution for his result-driven obviousness analysis is blatant use of inappropriate hindsight, and completely undermined the credibility of his obviousness analysis. *See, e.g.*, *Astra Aktiebolag v. Andrx Pharm., Inc.*, 222 F. Supp. 2d 423, 581 (S.D.N.Y. 2002), *aff'd sub nom. In re Omeprazole Pat. Litig.*, 84 F. App'x 76 (Fed. Cir. 2003) (finding hindsight when defendant's expert "incorrectly decided obviousness by choosing from a few references one element, and then picking and choosing other elements from other references, all with knowledge of the solution described in the [] patent"); *see also Allergan, Inc. v. Barr Labs., Inc.*, 501 F. App'x 965, 971 (Fed. Cir. 2013) (affirming nonobviousness where "district court found that [expert's] credibility was 'flawed on a fundamental level' and declined to assign any weight to his opinions" because the expert's "prevarication and inconsistency were repeatedly demonstrated during . . . cross examination") (internal quotation marks omitted); *Ferring Pharms. Inc. v. Fresenius Kabi USA, LLC*, No. 20-cv-431, 2022 WL 17584954, at *45 (D. Del. Dec. 12, 2022) (testimony of expert not credible because it "suffer[ed] from significant and improper hindsight bias").

346. The record reflects that Dr. Forrest "use[d] the challenged patent as a roadmap to reconstruct the claimed invention using disparate elements from the prior art." *TQ Delta, LLC v. Cisco Sys., Inc.*, 942 F.3d 1352, 1361 (Fed. Cir. 2019). This unabashed and unapologetic hindsight is exactly "the impermissible *ex post*

reasoning and hindsight bias that *KSR* warned against," *id.*, and irreparably tainted Dr. Forrest's obviousness analysis. Mylan cannot establish obviousness on the back of such testimony, let alone by clear and convincing evidence.

D. Objective Indicia Support the Conclusion that the Asserted Claims are Not Obvious

347. Objective indicia (a/k/a secondary considerations) of nonobviousness serve as "essential safeguards that protect against hindsight bias" in the obviousness analysis. *Liqwd, Inc. v. L'Oreal USA, Inc.*, 941 F.3d 1133, 1136-37 (Fed. Cir. 2019); *see also WBIP, LLC v. Kohler Co.*, 829 F.3d 1317, 1328 (Fed. Cir. 2016) ("The objective indicia of non-obviousness play an important role as a guard against the statutorily proscribed hindsight reasoning in the obviousness analysis."). As such, objective indicia of nonobviousness are "not just a cumulative or confirmatory part of the obviousness calculus but constitute[] independent evidence of nonobviousness." *Ortho-McNeil Pharm, Inc. v. Mylan Laby's., Inc.*, 520 F.3d 1358, 1365 (Fed. Cir. 2008); *see also Leo Pharm. Prods. Ltd. v. Rea*, 726 F.3d 1346, 1357-58 (Fed. Cir. 2013) ("[C]onsideration of the objective indicia is ***part of*** the whole obviousness analysis, not just an afterthought.") (emphasis in original). In other words, contrary to Mylan's contention during openings, Tr. 346:12-15, objective indicia are not part of a "burden-shifting framework;" the objective evidence must be considered as part of the obviousness analysis, for which the defendant bears the burden throughout. *See Cyclobenzaprine*, 676 F.3d at 1075-78;

accord Apple, Inc. v. Samsung Elec. Co., 839 F.3d 1034, 1048 (Fed. Cir. 2016) (en banc).

348. To be relevant to the obviousness inquiry, there must be "some causal relation or 'nexus' between an invention and [the objective indicia]." *Merck & Co. v. Teva Pharm., USA, Inc.*, 395 F.3d 1364, 1376 (Fed. Cir. 2005). "Questions of nexus are highly fact-dependent and, as such are not resolvable by appellate-created categorical rules and hierarchies as to the relative weight or significance of proffered evidence." *WBIP*, 829 F.3d at 1331; *see Apple*, 839 F.3d at 1055 ("It is within the province of the fact-finder to resolve these factual disputes regarding whether a nexus exists.").

349. Objective indicia include long-felt but unsolved need, expressions of skepticism, and commercial success. *See, e.g.*, *Apple*, 839 F.3d at 1052-53; *WBIP*, 829 F.3d at 1332-37. Based on the facts of record in this case, Janssen has established that all three of these objective indicia support the nonobviousness of the Asserted Claims.

350. **Long-felt need.** "The existence of a long-felt but unsolved need that is met by the claimed invention is . . . objective evidence of non-obviousness," *Millennium*, 862 F.3d at 1369, "because it is reasonable to infer that the need would have not persisted had the solution been obvious," *WBIP*, 829 F.3d at 1332. This is true here. There was a long-felt need for a longer-acting LAIA treatment with a

rigorous protocol for re-initiating patients who miss a dose and return for treatment after a certain period of time. FOF 215-220. The Asserted Claims met that need. FOF 220.

351. **Commercial success.** The commercial success of a claimed invention is an objective indication of nonobviousness where, as here, there is a nexus "between the evidence [of commercial success] and the merits of the claimed invention." *Novartis AG v. Torrent Pharm. Ltd.*, 853 F.3d 1316, 1330 (Fed. Cir. 2017). "It is not necessary, however, that the patented invention be solely responsible for the commercial success, in order for this factor to be given weight appropriate to the evidence" in an obviousness inquiry. *Cont'l Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1273 (Fed. Cir. 1991). In particular, nexus can be established with evidence that "customers would be less likely to purchase [a product] without" the feature enabled by the patented invention, even if there are also many other reasons for purchasing the product. *Apple*, 839 F.3d at 1055. For example, the Federal Circuit has held that there is a nexus between the slide-to-unlock feature of an iPhone and the commercial success of the iPhone, even though many other features contribute to the commercial success of the iPhone. *Id.* at 1054-56.

352. The record shows that Invega Trinza has been commercially successful, FOF 221-225, and that HCPs would have been less likely to prescribe

Invega Trinza without the missed dose re-initiation regimen set forth in the Asserted Claims. FOF 226-231. This evidence establishes a nexus between Invega Trinza's substantial commercial success and the Asserted Claims.

353. **Skepticism.** "Evidence of industry skepticism weighs in favor of non-obviousness." *WBIP*, 829 F.3d at 1335. It is undisputed that physicians were skeptical of the practical effectiveness of the innovative re-initiation regimen set forth in the Asserted Claims. FOF 239-240. Even today, some clinicians—including Dr. Berger—remain unconvinced about the wisdom or safety of the patented missed dose regimen. FOF 239. This evidence that experts were "skeptical about . . . the workability" of the unique regimen for patients who have missed a dose weighs in favor of non-obviousness. *WBIP*, 829 F.3d at 1335.

V. MYLAN FAILED TO PROVE THAT THE ASSERTED CLAIMS ARE INVALID FOR LACK OF ENABLEMENT

354. The 693 Patent is presumed enabled. *Cephalon, Inc. v. Watson Pharm., Inc.*, 707 F.3d 1330, 1337 (Fed. Cir. 2013). Mylan bears the burden to prove "by clear and convincing evidence that a person of ordinary skill in the art would not be able to practice the claimed invention without undue experimentation." *Allergan, Inc. v. Sandoz Inc.*, 796 F.3d 1293, 1309 (Fed. Cir. 2015) (internal quotation marks omitted). Mylan has failed to do so.

355. Mylan has exclusively argued lack of enablement in the alternative to obviousness, FOF 242-244, even though that is not necessary or required under

governing law. *See id.* at 1310 (rejecting defendant's argument that "if the asserted claims are nonobvious, they cannot possibly be enabled"). The test for each is different: "[t]he obviousness inquiry turns on what the ***prior art*** would have taught a [POSA] and whether the claimed invention would have been obvious in view of the prior art," whereas "the enablement inquiry turns on whether the skilled artisan, ***after reading the specification***, would be able to make and use the claimed invention without undue experimentation, based on the ordinary skill in the art." *Id.* Regardless of the reason for his alternative opinions, Mylan's expert did not endorse Mylan's non-enablement theory and did not hold an "abiding conviction that the truth of [the] factual contentions are highly probably," *see* FOF 242-244, as required to meet Mylan's burden of clear and convincing evidence. *ActiveVideo Networks, Inc. v. Verizon Commc'ns., Inc.,* 694 F.3d 1312, 1327 (Fed. Cir. 2012).

356. Mylan's enablement argument is limited to the terms PP1M and PP3M; it does not dispute that the missed dose dosing regimens themselves—the subject matter of the Asserted Claims—are enabled. FOF 245. Thus, Mylan must establish that a POSA cannot make and use PP1M and PP3M without undue experimentation in the context of otherwise enabled dosing regimens.

357. "Whether undue experimentation is required is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations [*i.e.*, the *Wands* factors]." *Cephalon*, 707 F.3d at 1336 (internal

quotation marks and citation omitted); *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). The so-called *Wands* factors can include:

> (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Cephalon, 707 F.3d at 1336 (quoting *Wands*, 858 F.2d at 737).

A. Mylan Did Not Provide Evidence that Experimentation is Required or That Any Formulation Is Not Enabled

358. Mylan failed to make two important threshold showings for enablement.

359. First, Mylan did not put forth ***any*** evidence that experimentation is needed to practice the Asserted Claims, let alone that such experimentation is "undue." FOF 273-275. The *Wands* factors are not "a generalized test for deciding whether a patent disclosure is sufficiently detailed to support a broad claim." *See Alcon Research Ltd. v. Barr Lab'ys, Inc.*, 745 F.3d 1180, 1189 (Fed. Cir. 2014). Rather, Mylan bears the burden to "put forward evidence that some experimentation is needed to practice the patented claim," and the "factors set forth in *Wands* then provide the factual considerations that a court may consider when determining whether the amount of that experimentation is either 'undue' or sufficiently routine such that an ordinary skilled artisan would reasonably be expected to carry it out." *Id.*

360. While Dr. Forrest suggested that "a lot" of testing would be required to determine if formulations were "within what is a PP1M or a PP3M," he failed to specify what that testing is, what it would entail, and whether such experimentation would be undue. FOF 273-275. Nor did he explain why testing was required at all to determine if a formulation "is a PP1M or a PP3M." FOF 273-275. The 693 Patent discloses the structural features of PP1M and PP3M and a POSA would have made a formulation pursuant to those features. FOF 274. There is no evidence that a POSA making PP1M and PP3M with those structural features would need to do any experimentation. FOF 273-277. Dr. Forrest's conclusory assertion that "a lot" of unspecified testing is necessary to practice the claims is insufficient as a matter of law to establish lack of enablement. *See Alcon*, 745 F.3d at 1189 (rejecting expert's "unsubstantiated conclusory statement" that "a lot of variables" meant that "the experimentation gets out of control quickly"). And Mylan's failure to show that any experimentation (let alone "undue experimentation") is necessary to practice the claims, *i.e.*, to make PP1M and PP3M and use them in the claimed dosing regimens, amounts to a failure of proof. *See id.* (concluding district court erred in enablement analysis because it did not address the determinative question of whether defendant showed that any experimentation was necessary to practice the claimed method).

361. Second, Mylan failed to identify a concrete example of a formulation of PP1M or PP3M that it contends falls within the Asserted Claims but cannot be made or used in the claimed dosing regimens without undue experimentation. FOF 279-281. The Federal Circuit has explained:

> Conducting the *Wands* analysis has routinely involved concrete identification of at least some embodiment or embodiments asserted not to be enabled—including what particular products or processes are or may be within the claim, so that breadth is shown concretely and not just as an abstract possibility, and how much experimentation a skilled artisan would have to undertake to make and use those products or processes.

McRO, Inc. v. Bandai Namco Games Am., Inc., 959 F.3d 1091, 1100 (Fed. Cir. 2020). Here, the enablement question is not a "concrete one," *id.* at 1101, because Mylan has not identified any formulation it contends is not enabled.[28] FOF 279-281.

B. The *Wands* Factors Support Enablement

362. Even if Mylan had established the type and manner of experimentation required to practice the Asserted Claims, it failed to establish by

[28] Although Dr. Forrest referred to a formulation in the 843 Patent as "problematic" for enablement and mentioned it in passing in his written description opinion, he did not establish, nor does the 843 Patent mention, (1) that it was a PP1M or PP3M formulation within the meaning of the 693 Patent, or (2) that it could not be made or used in the claimed dosing regimens. FOF 279-281. The 843 Patent is incorporated by reference in the 693 Patent as background information about paliperidone ester formulations. FOF 281; PTX-1 at 1:62-64, 9:31-43. To the extent a POSA would find any discrepancies between the two, the POSA would rely on the information in the 693 Patent and view the 843 Patent through that lens. FOF 281.

clear and convincing evidence that the amount of that unspecified experimentation was undue. The fact that some experimentation is required to practice a claim is not dispositive; to the contrary, even "a considerable amount of experimentation is permissible, if it is merely routine." *Cephalon*, 707 F.3d at 1399 (internal quotation marks and citation omitted).

363. Dr. Forrest testified that PP1M and PP3M are not enabled based on a subset of the *Wands* factors: the amount of direction or guidance in the specification, the presence or absence of working examples, the predictability of the art, the nature of the invention, the breadth of the claims, and the quantity of experimentation necessary. FOF 282. None of those factors alone or in combination establish that PP1M and PP3M cannot be made or used in the claimed missed dosing regimens.

1. The 693 Patent Provides Extensive Direction and Guidance, Including Exemplary Formulations

364. The *Wands* factors, including "the amount of direction or guidance presented" and "the presence or absence of working examples," support a finding of enablement. *Cephalon*, 707 F.3d at 1336 (quoting *Wands*, 858 F.2d at 737).

365. The 693 Patent provides extensive direction and guidance to a POSA as to how to make PP1M and PP3M and how to use them in the dosing regimen of the Asserted Claims, including a substantial recipe-like disclosure of ingredients, concentrations, and particle size, as well as detailed manufacturing instructions.

FOF 246-254. Moreover, the 693 Patent includes exemplary PP1M and PP3M formulations and identifies commercial embodiments thereof. FOF 255-258.

366. Although Mylan's expert suggested that there was insufficient guidance or examples to enable the full scope of the Asserted Claims, the "patent's specification need not 'describe how to make and use every possible variant of the claimed invention.'" *McRO*, 959 F.3d at 1100 (quoting *AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1244 (Fed. Cir. 2003)). Moreover, the 693 Patent did not need to lay out for a POSA every possible combination of excipients and concentration, because "[t]here is no requirement that a specification must disclose what is routine and well known in the art." *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1366 (Fed. Cir. 1997). Working with and switching between different excipients in a class (like wetting agents) is something that a POSA could do without undue experimentation. FOF 264.

367. The information in the 693 Patent is more than sufficient for a POSA to make and use PP1M and PP3M in the Asserted Claims without undue experimentation.

2. The Asserted Claims Are Not Broad

368. The "scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the

art." *In re Deuel*, 51 F.3d 1552, 1560 (Fed. Cir. 1995) (quoting *In re Fisher*, 427 F.2d 833, 839 (C.C.P.A. 1970)).

369. Here, the Asserted Claims are directed to missed dose dosing regimens with specific formulations, amounts, timing, and injection sites. *See* FOF 33-39. The Asserted Claims are not unduly broad, nor are the specific challenged terms—PP1M and PP3M. The parties agree that the specification discloses the structural features of PP1M and PP3M.[29] FOF 246. These include the ingredients, concentrations, and particle sizes of PP1M and PP3M. FOF 246-250.

370. Although Mylan's expert argued that even with the disclosure of the structural features, the Asserted Claims are "very broad," he failed to consider the breadth of the claims from the perspective of one skilled in the art. FOF 264, 267-272. *See Cephalon*, 707 F.3d at 1336 ("To satisfy section 112 . . . the specification must enable a ***person of ordinary skill in the art*** to make and use the invention.") (cleaned up).

371. Given the information in the 693 Patent, which amounts to a "recipe" for PP1M and PP3M, a POSA would not, as Dr. Forrest contends, view the scope of PP1M or PP3M as covering "well over 10 million possible combinations." FOF 260. Rather, a POSA would understand that individual formulations are commonly

[29] Mylan has not argued or presented any evidence that the Asserted Claims contain functional limitations, and Mylan has waived any arguments to the contrary.

described using classes of excipients and concentration ranges, rather than individual excipients, and using particle size ranges as opposed to a single particle size. FOF 261, 264-266, 268-272. Indeed, a POSA would understand this was standard and reasonable practice, particularly given that, as a scientific matter, particles in formulations ordinarily exist as a range of sizes. FOF 268.

372. [redacted] FOF 269-271. Thus, the terms PP1M and PP3M are not unduly broad and this weighs in favor of enablement.

3. Mylan Did Not Present Any Evidence About the Quantity of Experimentation

373. The quantity of experimentation is relevant to determining whether experimentation is undue. *Wands*, 858 F.2d at 737. Mylan failed to present any evidence about the quantity of experimentation.

374. The "question of undue experimentation is a matter of degree . . . . [E]xtensive experimentation does not necessarily render the experiments unduly extensive where the experiments involve repetition of known or commonly used techniques." *Cephalon*, 707 F.3d at 1338.

375. As discussed above, Dr. Forrest stated that "a lot" of testing would be required to determine if formulations were "within what is a PP1M or a PP3M" but he did not explain why any testing was necessary or what that testing would be. FOF 273-275. Accordingly, Mylan has not presented any evidence that the unspecified testing that Dr. Forrest alluded to was undue or anything other than routine. Mylan failed to "show that the resulting experimentation in this case would be excessive, *e.g.*, that it would involve testing for an unreasonable length of time" and thus failed to establish lack of enablement. *See Cephalon*, 707 F.3d at 1339.

376. In contrast, Dr. Little persuasively testified that, even if the terms PP1M and PP3M were understood to encompass tens of thousands of formulations, a POSA would be able to make any one of those formulations without undue experimentation for use in the Asserted Claims given the disclosure in the 693 Patent (including general and specific manufacturing instructions). FOF 261. This factor also weighs in favor of enablement.

* * *

377. In sum, Mylan has failed to meet its burden that the Asserted Claims are invalid for lack of enablement by clear and convincing evidence. Mylan did not identify any specific formulation that it contends cannot be made or used without undue experimentation and failed to provide evidence that any specific experimentation was required, much less that it was undue. The specification of the

693 Patent contains ample guidance and examples for a POSA to make and use the full scope of the Asserted Claims.

VI. MYLAN FAILED TO PROVE THAT THE ASSERTED CLAIMS ARE INVALID FOR LACK OF WRITTEN DESCRIPTION

378. Mylan also bears the "burden of establishing by clear and convincing evidence that the [written description] requirement was not met, in light of the presumption of validity." *Intirtool, Ltd. v. Texar Corp.*, 369 F.3d 1289, 1294 (Fed. Cir. 2004).

379. A patent must have "a written description of the invention," 35 U.S.C. § 112(a), which "clearly allow[s] persons of skill in the art to recognize that the patentee invented what is claimed." *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc).

380. The test for written description "is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Id.* Stated simply, the question is whether the claims correspond to what is described in the specification. *Alcon*, 745 F.3d at 1191. This test "involves 'an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art.'" *Immunex Corp. v. Sandoz, Inc.*, 964 F.3d 1049, 1063 (Fed. Cir. 2020) (quoting *Ariad*, 598 F.3d at 1351).

381. Mylan's cursory written description challenge, which mirrors its enablement argument, is insufficient. Mylan does not dispute that the missed dose dosing regimens of the Asserted Claims—the subject of the 693 Patent—are adequately described in the 693 Patent or that the inventors possessed the subject matter that is the missed dose regimens. FOF 287. Mylan contends only that the terms PP1M and PP3M lack written description based on what it characterizes as a broad scope of the terms and a dearth of working examples of PP1M and PP3M. FOF 287.[30]

382. Mylan failed to meet its burden of clear and convincing evidence. A POSA reviewing the "four corners of the specification" would understand that the inventors were in possession of the subject matter of the claims, including PP1M and PP3M. *Ariad*, 598 F.3d at 1351. There is no dispute that the 693 Patent specification unambiguously identifies not only the claimed invention—the missed dose regimens—but also sets out structural features for both PP1M and PP3M.

[30] Dr. Forrest also mentions in passing in his written description opinion that the 843 Patent discloses a formulation with a 5 µm particle size (which Dr. Forrest asserts is PP1M), and he suggests that this contradicts the 693 Patent's description of PP1M and PP3M. FOF 287. But the 843 Patent does not state whether any of its formulations are PP1M or PP3M within the meaning of the 693 Patent. FOF 280-281. Mylan's and Janssen's experts agree that the 693 Patent unequivocally defines the structural parameters of the PP1M and PP3M formulations of the 693 Patent. FOF 280 n.23. And if there were a discrepancy between the 693 Patent disclosure and an earlier patent incorporated by reference in the 693 Patent, the 693 Patent disclosure would govern a POSA's understanding of the terms PP1M and PP3M. FOF 281.

FOF 246, 259. Those structural features include a recipe-like disclosure of the ingredients, concentrations, and particle sizes for PP1M and PP3M. FOF 246-250. Moreover, the 693 Patent discloses preferred examples and identifies commercial embodiments. FOF 255-258.

383. The Federal Circuit has "repeatedly 'explained that an adequate written description requires a precise definition, such as by ***structure***, formula, chemical name, physical properties, or other properties . . . sufficient to distinguish the genus from other materials.'" *GlaxoSmithKline LLC v. Banner Pharmacaps, Inc.*, 744 F.3d 725, 730 (Fed. Cir. 2014) (emphasis in original) (quoting *Ariad*, 598 F.3d at 1350) (concluding that description of structural features of molecular complex was sufficient written description).[31] That is precisely the case here, where the 693 Patent provides structural features that would allow a POSA to "visualize or recognize the identity of the subject matter purportedly described," namely PP1M and PP3M, and to distinguish it from other materials. *See Alcon*, 745 F.3d at 1190 ("written description requirement is met when the disclosure allows one skilled in

[31] Mylan has not argued or presented evidence that the Asserted Claims are defined by functional claim language, where written description issues sometimes arise when claims "cover any compound later actually invented and determined to fall within the claim's functional boundaries" or "merely recite a description of the problem to be solved while claiming all solutions to it." *Ariad*, 598 F.3d at 1353. The terms PP1M and PP3M are defined in the 693 Patent by structural features, which are adequately described.

the art to visualize or recognize the identity of the subject matter purportedly described").

384. Mylan does not dispute that the 693 Patent discloses the structural features of both PP1M and PP3M, nor does it dispute that a POSA would be able to visualize or recognize the PP1M or PP3M formulations as described in the 693 Patent. FOF 246, 259. Instead, Mylan contends that the 693 Patent does not contain sufficient examples or known formulations to demonstrate possession of the entire claimed range. FOF 287. For the reasons described in connection with enablement, Mylan failed to establish that the scope of PP1M and PP3M was unduly large. FOF 368-372.

385. Moreover:

> There is no requirement that the disclosure contain 'either examples or an actual reduction to practice'; rather the critical inquiry is whether the patentee has provided a description that 'in a definite way identifies the claimed invention' in sufficient detail that a person of ordinary skill would understand that the inventor was in possession of it at the time of filing.

Alcon, 745 F.3d at 1190-91 (citations omitted).

386. To the extent that Mylan contends that the Asserted Claims are invalid because they are broader than the examples disclosed, Mylan is incorrect: "a patent claim is not necessarily invalid for lack of written description just because it is broader than the specific examples disclosed." *Martek Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1371 (Fed. Cir. 2009).

387. On the question of whether the 693 Patent demonstrates that the inventors were in possession of the "full scope" of what constitutes PP1M and PP3M as described in the 693 Patent, there is no doubt that they did. The inventors described the structural features of those formulations in detail in a manner that a POSA would understand and use to visualize or recognize the formulations. FOF 246-258. Thus, "[t]he claim is no broader in scope than the written description" and Mylan's written description argument fails. *GlaxoSmithKline*, 744 F.3d at 731-32.

VII. MYLAN FAILED TO ESTABLISH THAT THE ASSERTED CLAIMS ARE INVALID UNDER 35 U.S.C. § 101

388. Although Mylan's pretrial submission included law concerning patent ineligible subject matter under 35 U.S.C. § 101, *see* JPTO at 113 ¶¶ 41-42, Mylan presented no evidence or argument at trial regarding alleged invalidity of the Asserted Claims for claiming patent ineligible subject matter.

389. Because Mylan failed to present a defense based on patent eligibility at trial, Mylan has waived any such defense and failed to meet its burden of proving it. *See Vanda*, 887 F.3d at 1337-38 (finding written description challenge waived "by failing to properly present it to the trial court"); *Asetek*, 100 F. Supp. 3d at 893-94 (indefiniteness defense waived and failed where not properly presented at trial); *Fractus, S.A. v. Samsung Elecs. Co.*, 876 F. Supp. 2d 802, 838-39 (E.D. Tex. 2012) (holding similar).

390. Furthermore, Mylan concedes that the Asserted Claims are methods of treatment. *See, e.g.*, JPTO at 50 ¶ 22, at 74 ¶ 98 (Mylan asserting that "[t]he asserted claims recite method of treatment claims"); Tr. 393:15-22 (Forrest); Tr. 477:2-5 (Forrest) (describing claim 10 as "a method claim").

391. The law is clear that "claims that are directed to particular methods of treatment are patent eligible." *Natural Alternatives Int'l, Inc. v. Creative Compounds, LLC*, 918 F.3d 1338, 1344 (Fed. Cir. 2019); *accord Vanda*, 887 F.3d at 1134. Any Section 101 defense would therefore fail.

VIII. MYLAN'S DIVIDED INFRINGEMENT DEFENSE IS UNTIMELY

392. Local Patent Rule 3.6 sets forth disclosure requirements for patent cases arising under the Hatch-Waxman Act, including the disclosure of "Non-Infringement Contentions and Responses" from a "party opposing an assertion of patent infringement." L. Pat. R. 3.2A, 3.6(g).

393. "Local Patent Rules exist to further the goal of full and timely discovery and provide all parties with adequate notice and information with which to litigate their cases," as well as to "require parties to crystallize their theories of the case early in the litigation and to adhere to those theories once they have been disclosed." *Celgene Corp. v. Hetero Lab'ys*, No. 17-cv-3387 (ES)(MAH), 2021 WL 3701700, at *19 (D.N.J. June 15, 2021) (internal quotation marks and citation omitted).

394. Mylan's divided infringement theory was not disclosed in its contentions. FOF 64. It was disclosed for the first time in Mylan's rebuttal expert report. FOF 64. That is improper. *See, e.g.*, *Chiesi United States v. Aurobindo Pharma United States*, No. 19-cv-18756 (ZNQ)(LHQ), 2022 WL 304574, at *4-5 (D.N.J. Jan. 9, 2022) (granting motion *in limine* precluding testimony on indefiniteness theory that was not disclosed in contentions); *Merck Sharp & Dohme Corp. v. Sandoz, Inc.*, No. 12-cv-3289 (PHS)(LHG), 2014 WL 997532, at *9 (D.N.J. Jan. 6, 2014) (striking portions of expert reports that rely on prior art not disclosed in contentions); *Celgene*, 2021 WL 3701700, at *17 (striking invalidity theory "not set out" in contentions because it is "impermissible" to introduce new theories in an expert report without amendment).

395. Because Mylan did not properly disclose its divided infringement defense in its contentions, and because Mylan has not sought to amend its contentions to add such a defense, Mylan's divided infringement defense is untimely and should therefore be stricken. *Chiesi*, 2022 WL 304574, at *4-5.

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CERTIFICATE OF SERVICE

I certify that on January 24, 2023 I caused true and correct copies of Plaintiffs' Proposed Findings of Fact and Conclusions of Law to be served via e-mail on all counsel of record.

/s/ Keith J. Miller
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